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### Nutrition and Human Reproduction: An Historical Review

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I HAVE chosen for the subject of my address an historical review of nutrition and reproduction. With full realization that I cannot qualify as an historian, a physiologist, or a trained nutritionist, I venture to pass on to you certain fancies and facts relating to nutrition and reproduction. The early history of nutrition in pregnancy is sketchy and the opinions expressed relating to food and pregnancy are unscientific and in many instances undesirable or even harmful. However, the experience in practical nutrition derived from observation and the trial and error method has led to the scientific and practical phases of nutrition in general and their application to pregnancy which have been developed in the first half of this century.

At the outset it is in order to define the term "nutrition," which is described in Webster as "the sum of the processes by which an animal or plant absorbs, or takes in and utilizes, food substances." Nutrition in pregnancy in reality embraces all that is implied in the use of the term "reproduction," which includes fertilization, nourishment of the embryo, growth and development of the fetus, and, as a corollary, the fitness and health of the mother. Food requirements depend on age, sex, climate, physical activity, and racial food habits, and it becomes obvious that the requirements change in the course of pregnancy and lactation.

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Man's most compelling instincts are self-preservation and reproduction. Man's continued presence on this planet is predicated on his ability to continue to exist and to reproduce his kind. It is evident that food in the broad sense is of primary importance to the individual and to the species; without nutrition life cannot continue; without continuity of life and reasonable health there can be no self-defense; without these two, reproduction of the species ceases. Food has played a primary role in the survival and development of man. Probably it is the most important factor in reproduction.

Ancient writings, including the Old Testament of the Bible, contain many instances of laws and admonitions concerning foods. However, these have a general application to a people or tribe, and there is a paucity of dietary advice to the pregnant woman. More information concerning nutrition and reproduction can be obtained from a study of the customs and taboos of the American Indians, the Eskimos, and the present-day tribes and races in Africa and the South Sea Islands.

However, some records of ancient writings survive. In Papyrus Ebers,[5] circa 1500 B.C., a collection of bits and pieces of Egyptian folklore translated by H. Joachim, there are passages relating to the pregnant woman. "To produce milk, mix fragrant bread made from soured durra (a variety of millet) with the ground poppy plant and require the parturient to sit crosslegged while eating it." Another passage relates to the treatment of protracted labor by applying peppermint to the bare posterior of the parturient woman—*vis a tergo,* so to speak.

Hippocrates is credited with the statement that women should use a regimen of rather dry food, for, he said, food that is dry is more adapted to the softness of their flesh and less diluted drinks are better for the womb and for pregnancy. He also sagely remarked that foods and drinks that are not quite so good are to be preferred, if only they are more agreeable. If a pregnant woman eats suckling pigs, the fetus will have weak joints and will be subject to diseases of the joints. Constantine is quoted as having wisely recommended that any food which is not near at hand or easily procurable should not be mentioned in the presence of a pregnant woman. If her desire [for food] is kindled and unsatisfied, there is danger that the uterus may sink down.

One bit of advice attributed to ancient Rome is that the burden of the parturient woman will be dispelled before the onset of labor if at that time she has eaten the flesh of wolves or if a woman who has tasted wolves' flesh that day attends the birth. Shades of Romulus and Remus! If a woman has eaten young stork, ophthalmia is prevented, the eyes are made clear and the child even surpasses the mother. A mother who wishes her child to have black eyes should frequently eat mice.

Opinions concerning the nutritional value of milk varied. It was said to be the most nourishing of all liquids used as food, but oddly enough, it was supposed to cause teeth to decay and kidney stones to develop. Another saying advised that, if a pregnant woman greatly desires milk, it should be boiled with salt water and a little sugar and the scum removed before drinking. Galen advised that milk with honey drunk by the parturient causes the uterus to sink

down gently. One suggestion of significance was that, if fresh milk is drunk after childbirth, it makes the breasts secrete more abundantly.

If partridge eggs are eaten, they produce fertility and an abundance of milk. After Juno ate wild lettuce she conceived her daughter, Hebe, although formerly she had been sterile. Lettuce was said to have the greatest nourishing power of all vegetables, cooling and soothing the stomach, stimulating appetite and elimination, and promoting sleep. This sounds like a modern radio plug!

According to Nixon, in the Chou Dynasty, 1155 B.C., pregnant women were warned to be careful in the selection of their food; that, among other foods, goat meat would produce a sickly child, turtle meat a child with a short neck, and, aptly enough, that donkey meat would cause the woman to go over time and have a difficult labor. Perhaps the author had been irked by a stubborn donkey.

The continued existence of man through the periods of Greek and Roman ascendancy and the Dark Ages indicates that a diet sufficient for survival and reproduction must have been known and available during these times, although only meager writings on diet in pregnancy are extant. In *Priests of Lucina,* Findley quoted Albertus Magnus, a friar of the thirteenth century, who cautioned against mentioning injurious foods in the presence of the pregnant woman, for to deny her any food she may desire might cause the unborn child to die of weakness. In a treatise by Pratis, kindly translated from the Latin for me by Dr. John Miner, Constantine is said to have made a somewhat similar statement. In the *Rosengarten* of Eucharius Rösslin, A.D. 1513, there are colored drawings of the development and position of the fetus and its delivery but no mention is made of diet.

In 1767, Zückert wrote a treatise devoted almost exclusively to dietary advice to the pregnant woman. In this occurs the first mention I have found of avoidance of salt, contained in his admonition to pregnant women to avoid salty, acrid, sour foods, eggs, and all greasy foods that have stood long in copper kettles. It is noteworthy that he does not forbid digestible meat. In the matter of diet he divided pregnant women into three groups: 1. The peasant class who were healthy and strong on a diet of pumpernickel (bread made of coarse rye), ammunition bread (also a dry black bread for troops in the field), cheese and tough meat. He stated that this food agreed with these women because of good digestion derived from simple living and physical work. 2. Those women of a more leisurely group, "commonly city dwellers and those in the upper classes with weakly bodies and stomachs, tender sensitive nerves who commonly eat anything their appetite demands." 3. Women with aversion to food or those with gastritis and atonic stomachs. He recommended common bread (no doubt made with whole grain), greens, and simply prepared foods, and agreed with the free choice of other eatables, except harmful foods; he urged moderation in eating. He wisely remarked, "It is a great pity [that moderation] does not please those who concede absolute power to their senses." Pregnant women "who eat well and digest much are plethoric and this is the more dangerous to pregnant women who have no work and exercise." He advised the pregnant woman to "eat little and not late." He warned against the extensive use of tea or coffee because too much warm fluid relaxed and softened the stomach and intestines, which "become

like the withered skin of the hand of the laundress." Surprisingly enough, for those times, he lauded plain water, calling it "the sacred drink of the ancient patriarchs," but he warned, "water chills and burdens stomachs unaccustomed to it." Although he said milk was advisable for women with good stomachs, he recommended beer, asserting that beer has more power than merely to quench thirst, thin the blood, and strengthen the body; and he stated, "no one will persuade the world that a glass of good, pure wine has hurt anybody when taken in moderation." Coming into modern times, Drummond, quoted by Nixon, stated that malnutrition was more rife in England in the beginning of the present century than in medieval times.

It is known that even prior to 1850 the diet of some pregnant women was being restricted in order to lessen the size of the fetus, for Cazeaux, in his treatise on midwifery of that date, stated that he did not agree with this recommendation. Naegele, in 1853, advised two rules for pregnant women, first that small, frequent meals were better than one or two large, protracted meals, and second, that salty, spicy, sour foods should be avoided. In the nineteenth century and even in early years of the twentieth, it was more or less customary for recently delivered women to be placed for a day or two on very limited diets similar to those given to patients after laparotomy. Atkinson, in 1879, wrote that this was not sound reasoning and that the diet of the recently delivered woman should be guided by her appetite and her general condition. Burnett, of London, England, also was in advance of his time when in 1880 he wrote on the prevention of harelip, cleft palate, and other congenital defects by medicinal and nutritional treatment of the mother during pregnancy. A keen observer, he stated with outspoken expression and vigorous criticism, "The child of the well-fed, well-worked, cheerful, happy woman living in a sunlit, airy habitation, is at birth the finest specimen of its kind. On the other hand, what a miserable sight do the newborn babies of our courts and alleys, and of the pampered, tight-laced, high-heeled, lazy, lounging, carriage-possessing women of the high classes present: The extremes meet, the poor, blanched creature, half-starved, over-worked, shut in some close sunless dwelling brings forth her fruit very like that of the pale-faced, over-fed, under-worked, sofa-loving sister of the mansion and of the palace."

It is evident that all was not well with the dietary habits of the general population and incidentally of pregnant women in Europe in the so-called era of growing enlightenment of the eighteenth and nineteenth centuries. Life in the towns and cities had become more sheltered and many people had forgotten much of the knowledge of what to eat and what not to eat—food habits, if you like, acquired by primitive people in their keen and continuous struggle for survival. Much has been learned from century-old taboos and customs of primitive people which are being followed today among tribes in Africa and the South Sea Islands and among certain groups of Eskimos and natives of South America. The Eskimos on their natural diet of fish, seal oil and meat, animal organs, moss and roots and bulbs of water plants, maintained normal health, normal bony development, and normal teeth, but with the advent of highly milled flour, polished rice, and the canned foods of civilization their general health was lowered and dental caries and pyorrhea became evident.

In the course of his investigation of the nutritional factors associated with the development and maintenance of the teeth, Price found that most of the primitive tribes had evolved a balanced diet, containing adequate calories, a proper balance between proteins, fats, and carbohydrates, and sufficient vitamins and minerals. He noted that among the Masai, a hunting tribe of East Africa, each child and pregnant woman received daily a special ration of blood, along with milk and meat. A neighboring tribe, the Kikyu, an agricultural people, had a special diet for women during pregnancy and lactation, consisting of sweet potatoes, corn, beans, bananas and kaffir, a variety of millet. Many of these people attained advanced years without dental decay, pyorrhea, or the loss of teeth.

Most of the tribes among the American Indians lived on wild game, chiefly the internal organs and bone marrow, with maize and some vegetables and, in winter, the bark and buds of trees; much of the muscle meat was fed to dogs. Among some Indian tribes it was customary for the husband to go on a five-day fast after his child was born. This may have been done to permit his squaw to have more food in times of scarcity. With the advent of the reservation life and the benefits of modern civilization and its food there was a decided decrease in normal births and an increase in neonatal mortality rate. However, in recent years, with the adoption of the newer scientific knowledge of dietary requirements, improvement has occurred.

Diets vary in different localities, depending on climate, topography, and availability of dietary essentials; for example, in isolated Swiss valleys an almost normal diet is maintained on whole rye bread, dairy products, various fresh vegetables in season, stored vegetables in winter, and meat once a week. However, the lack of iodine in the ground water and drinking water in many localities resulted in endemic colloid goiter; under these conditions pregnant women often gave birth to cretins. Dental caries is notoriously common among the urban Scots and yet in the islands of the outer Hebrides there is little dental caries; the food consists of oat products, a few green vegetables and sea foods, including fish livers, a meager but balanced diet.

In China, bones boiled in dilute acids until they were soft were a dietary delicacy, no doubt owing to the prevalent lack of calcium and phosphorus; this lack no doubt inspired the gift of pigs' feet to the expectant mother. The Lapps remain well on a meager diet when it is supplemented by two or three ounces of fish oil daily. Among our early pioneers, pushing westward through the Middle Western states, pregnant women and children became ill and many died from "milk sickness," as did the cattle which ate richweed or white snake root.

Approximately fifty years ago a controversy over maternal nutrition and its effect on the size of the fetus arose among obstetricians, which awakened interest in maternal diets. In an ambitious attempt to reduce the weight of the baby and in particular the size and consistency of the fetal head, Prochownick[35] in the eighties of the last century carried thirty-one patients through thirty-six pregnancies, during the last six weeks of which their diet consisted of an increased amount of protein with a decided decrease in carbohydrates and fluids. He did not claim to reduce the size of fetal bones or retard ossification but to

reduce fat tissue, resulting in thinness and slackness of the subcutaneous tissues of the skin covering the head, which, he said, increased mobility of skull bones against each other and facilitated moulding.

As a result of sheer persistence and assertive publications, Prochownick[34, 35] extended the use of this diet, which I previously mentioned as having been rejected by Cazeaux in 1850, until it became known as the "Prochownick diet." In the course of the ensuing thirty or more years there was much controversy among the medical profession, obstetricians in particular, relative to the effect of this diet on the fetus and to its relief of dystocia. Lahmann, in 1893, advised a dry diet, with a minimum of salt and with limited calories, which he said produced smaller babies, fewer operative procedures, and less fetal injury. Later many well-known obstetricians, for example, Williams,[51] Cragin (quoted by Paddock), Hirst (quoted by Paton), Slemons, Edgar, Cornell, Rucker, and others, went into print with statements in favor of Prochownick's claims, while Reed (quoted by Oldham), Landau, Ehrenfest, and others opposed them. Ahlfeld (quoted by Oldham) agreed with Baumm that growth and development of the fetus in utero are influenced only by race and constitution of both parents, by heredity, and by the sex of the fetus, unless the diet is totally inadequate. However, opinion remained divided concerning the practical value of attempting to reduce the weight of the fetus by reducing the maternal diet; the possible importance of fetal weight reduction has waned since increased accuracy of roentgenologic pelvimetry and improvement in the technique of cesarean section have solved the problem of dystocia in most instances.

Among the early writers, Paton, in 1903, Murlin, in 1917, and Ehrenfest, in 1919, gave clear and searching analyses of the then known effect of nutrition on maternal health, labor, and the fetus. These writings and many other factors contributed to stimulate research in nutrition in the twentieth century.

A vast amount of thought and research has been devoted to nutrition in its relationship to reproduction. It is evident that we are too close to much of the investigation relating to this subject to evaluate its historical significance accurately. To attempt to enumerate all of the many excellent articles and research projects would place us in the position of the explorer who could not see the beauty of the woods because of the trees around him. It would be premature even to try to evaluate all of the findings and claims of various workers. Nor shall I attempt to give a chronologic description of the results of these investigations, but rather to present, as nearly as possible, the present-day consensus of investigators, nutritionists, and obstetricians concerning the relationship of food and its various elements to the well-being of the mother and the normal development and health of the fetus.

Our interest centers on the dietary requirements of the pregnant woman and her fetus. In this consideration of the immediate dietary requirements of the pregnant woman it must be borne in mind that the diet of a given generation may affect the offspring several generations hence. In other words, a woman may remain well on a diet which will prove to be inadequate under the added physiologic demands of pregnancy so that her offspring may suffer in development and in capacity to reproduce their normal kind.

I shall refrain from discussing the fetal-maternal relationship and the pertinent question first asked by Harvey: Does the placenta act by digestion or in a purely mechanical manner? Adequate exposition of this question is not feasible at this time. It may be stated that the initial period of pregnancy is one of parasitism. However, the nutrition of the fetus is not all obtained by simple diffusion, supporting the idea of active selective absorptive properties on the part of the placenta.

It is well known that the constituents of food are protein, fat, carbohydrate, water, minerals—including calcium, phosphorus, magnesium, iron and iodine—and vitamins—including fat-soluble A, D, and E, and water-soluble B-complex and C. Protein is the most important ingredient of food because it is the basic material for building tissue; fat is especially necessary as a solvent of vitamins A, D, and E; carbohydrates furnish most of the total calories and are the most readily accessible fuel for heat and energy production.

The nutritional requirements of an individual pregnant woman depend on heredity, environment, previous status of nutrition, weight, stage of pregnancy, and physical activity. It may be said that a pregnant woman's nutritional requirements are the same qualitatively as those of the nonpregnant, but that she requires more of everything, particularly protein, calcium, phosphorus, iron, iodine, and the vitamins. Too often her increased appetite has been satisfied by increased consumption of carbohydrates. Contrary to the opinion which prevailed as recently as two or three decades ago, that protein foods should be restricted during pregnancy, it is now held that the protein intake, which is at least 60 Gm. daily for the average woman, should be increased during pregnancy to a minimum of approximately 90 Gm. daily. There should be sufficient fat in the diet to act as a carrier of vitamins A and D and sufficient carbohydrates to reinforce the calories obtained from protein in order to produce energy and maintain proper weight.

McCarrison has pointed out that the Commission of the League of Nations advises the proportion of animal to vegetable protein as approximately 3 to 2. Animal protein includes that obtainable from meat, eggs, sea food, poultry, milk and cheese, while vegetable protein is furnished by legumes, other vegetables, bread and cereals. Certain proteins, namely beef, eggs, lactalbumin, and the glutenin of wheat, contain all of the essential amino acids. Milk appears to be a stabilizing factor in the human diet in civilized countries.

As amino acids, protein passes through the placenta by diffusion, but the fetal plasma at term has a higher percentage of amino acid nitrogen than the mother's plasma, suggesting a fixation method in the fetus which may control retention by the fetus of the amino acids. Ordinarily adequate maternal diet permits the storage of nitrogen, which begins as early as the tenth week of pregnancy and marks the state of positive nitrogen balance.

In 1933 Mellanby suggested that toxemias of pregnancy may be caused by inadequate diets, particularly of proteins and vitamins. Strauss stated that some toxemias could be traced to an inadequate intake of protein over a number of years. Protein calories need not exceed 10 per cent of the total calories, except under certain environmental and racial conditions, for example, in the

case of the Eskimos, who may consume 250 to 300 Gm. of protein daily. Ninety grams of protein are insufficient to meet the daily caloric requirement and the remainder is furnished by fat and carbohydrate food. Carbohydrates, about 250 Gm. of which are consumed daily, are protein-savers and furnish 50 to 60 per cent of the daily caloric intake. The amount of carbohydrate ingested needs control, because its excessive use results in undue storage of fat in the body tissues.

Fats ordinarily provide 35 per cent of the calories of the normal diet, furnishing about 100 to 140 Gm. daily. Fats are an additional source of energy, but their major role is to assist in the utilization of calcium and phosphorus and the fat-soluble vitamins, A, D, E and K. The maternal blood has a higher lipoid content than the fetal blood. The appetite for food is increased among pregnant women and there is a still greater demand among lactating women. The storage of nitrogen in a pregnant woman, in addition to forming reserve for nitrogen loss, increases her ability to lactate. Voluntary consumption of food may be 60 per cent greater among lactating women than during pregnancy.

The story of calcium is opened by the significant need for an adequate maternal storage of calcium. The fetus demands and gets calcium from the mother even if her diet is deficient; therefore, the prevention of calcium deficiency in the newborn is a problem for the obstetrician to solve by prenatal dietary measures. Phosphorus and calcium go together as the Damon and Pythias of diet. Phosphorus, as well as calcium, is activated by vitamin D and sunlight and is essential in the laying down of the bony framework and dental foundation in the fetus. It is claimed that a high mineral diet appears to be of value in developing relative immunity of the fetus to infection.

Iodine is concerned with metabolism and the maintenance of cell structure; its richest source is in sea food and in vegetables grown near the seashore. Its deficiency in the maternal diet is associated with the production of colloid goiter in the mother and of colloid goiter and, in cases in which the deficiency is extreme, with cretinism in the fetus.

Ingestion of iron is important. The pregnant woman has a relative anemia owing to blood dilution resulting from 20 per cent increase in blood volume. It is important that an iron deficiency or hypochromic anemia does not develop during pregnancy because of its effect on maternal health and for fear a similar delayed anemia will develop in the infant from the age of 2 to 6 months. An iron deficiency may develop as a result of protein deficiency. To avoid this type of maternal anemia the pregnant woman's minimal diet should contain approximately 90 Gm. of protein daily, plus adequate liver, and, when possible, such foods as apricots, egg yolk, cooked mustard greens, oysters, green vegetables, prunes, peaches, pineapple, orange and grapefruit.

## Water Balance

It has been suggested that 1.0 c.c. of water should be ingested for each food calorie. Aside from the water in food, this would require seven to eight glasses daily; approximately 2 quarts of fluid are dispersed from the skin and lungs and alimentary tract and 1½ quarts by the kidneys. A positive water balance ob-

tains in pregnancy and normally about 10 pounds of the gain of weight in pregnancy are owing to this water retention. Slemons has shown that the urinary output of the adult male represents 90 per cent of the fluid intake, primiparas voided 72 per cent of fluid drunk, multiparas 48 per cent, and multiparas with the fetus dead in utero voided an average of 93 per cent of the fluid drunk. Impaired excretion of sodium causes undue water retention and this appears to be a factor in the etiology of toxemia. For this reason a low salt diet is advised.

## Vitamins

The role of the vitamins in nutrition, now well known, is so broadly advertised "across the land," that, to paraphrase an old saying, he who speeds may read. We are advised to take vitamins to prevent this or that or to cure the other. Nutritionists state that a balanced adequate diet furnishes sufficient vitamins for the average person. However, in no other field of nutrition is the value of vitamins so clearly shown as in pregnancy. Researches have revealed various vitamins as the cause of diseases which baffled physicians and investigators for many years; lack of sufficient vitamin C as the cause of scurvy, deficiency of vitamin D and its accompanying minerals, calcium and phosphorus, in rickets and osteomalacia, deficiency of vitamin B in beriberi, of B-complex in pellagra, of vitamin A in night blindness and of vitamin E in sterility in rats. Sherman[39, 40] has stated that lack of vitamin E in male rats produces sterility and eventually leads to destruction of germ cells. Shute[41-43] has stated that lack of vitamin E is a factor in abortion and abruptio placentae.

Among the vitamins, A is essential to reproduction and fetal growth and its maternal lack is related to deficiency diseases and perhaps lowers immunity to infection, predisposing to puerperal sepsis. McCollum has stated that the supplementary administration of vitamin A tends to decrease the severity and frequency of colds. A vitamin A level sufficient for maternal health may, however, result in disaster for the offspring; for example, the teeth of the mother are less affected than those of the offspring. Vitamin A is inactivated by rancidity, by exposure to ultraviolet irradiation and to heat in the presence of oxygen. Carotene and vitamin A are poorly absorbed from the intestine whenever fat absorption is defective and in the presence of mineral oil laxatives.

Vitamin B is frequently lacking in the diet of American women, its lack in prenatal diet being evidenced by anemia, anorexia, irritability, and emotional instability, and in the presence of more severe deficiencies, by beriberi or by pellagra. A mother who has latent beriberi may bear a child who has congenital malformations. It has been shown that rats with riboflavin ($B_2$) deficiency may have repeated pregnancies resulting in severe fetal malformations. The synthesis of B vitamins by intestinal bacteria has a vital role in man and animals but in man supplementary dietary intake of B vitamins is necessary. The bacterial synthesis in the bowel may be suppressed by the administration of drugs, such as the sulfonamides, particularly when the therapy is protracted. Vitamin B is abundant in many foods, particularly meat, milk, and eggs. In the presence of known or suspected B deficiency the diet may be supplemented by yeast, yeast concentrates, and wheat germ. It was not until recently that the re-

searches of Warkany and others emphasized the importance of a reasonably adequate protein content as well as certain vitamins, particularly A and B, in the normal development of the fetus in rats. Warkany has stated that the organogenesis of the human embryo is practically finished at ten weeks after conception, whereas nutritional supplements usually are not given until the latter half of pregnancy.

There is a widespread belief among laymen and many physicians that systemic and multiple congenital malformations are always the result of defective germ plasm which is genetically determined or hereditary. Perhaps a nutritional deficiency resulting in a defective gene leads to the same congenital abnormality.

Ascorbic acid (vitamin C) is recognized to be decidedly important to normal reproduction. It is, of course, well known that it occurs abundantly in citrus fruit and tomatoes. The fetus has the faculty of taking its needed vitamin C from the maternal circulation, so that vitamin C in the maternal plasma may be lower than in the cord blood. A decidedly low level of ascorbic acid in maternal plasma within the range of clinical scurvy has been noted in severe cases of hyperemesis. Tompkins has remarked that the vitamin C content is low in artificially ripened citrus fruit picked green for shipping purposes.

I have stated previously that normal reproduction requires adequate amounts of protein in the diet, that the ingestion of protein should be increased during pregnancy, particularly in its latter half, and that there should be a still greater increase of protein in the diet of the lactating woman. This statement is made advisedly because authorities on nutrition agree that protein is the most important component of the diet during pregnancy. A protein-poor diet is a common fault among pregnant women. Burke's statement is borne out by Williams,[50] Tompkins,[48] and many others, that malnutrition of protein and other substances in pregnancy results in a lower average hemoglobin and serum protein, a higher incidence of pre-eclampsia, a strikingly higher incidence of edema, increased maternal morbidity, and an increased fetal mortality rate. The observations of Theobald[46, 47] on the role of calcium, iron, and iodine, of De Snoo on salt as a prime factor in the production of pre-eclampsia, of Strauss, and many others well merit careful study.

Normal increase of weight during pregnancy amounts to 14 to 20 per cent of the pregravid weight. This is owing largely to an increase of body nitrogen and fat, retention of water, including increased blood volume, tissue fluid retention, and amniotic fluid. The pregnant woman stores nitrogen in the uterus and other tissues as a reserve against nitrogen depletion in the course of labor and lactation.

It appears that excessive gain of weight during pregnancy is owing to undue retention of fluid in the tissues and often to the excessive storage of body fat. Time does not permit full discussion of the causes of edema during pregnancy, including increased intracapillary pressure, lowered serum proteins and undue retention of the sodium ion. The prenatal diet often is too high in carbohydrates and various sodium salts and too low in protein, vitamins, and alkaline minerals.

When hypoproteinemia is present, signs of toxemia have been produced by feeding various sodium salts. In the absence of hypoproteinemia, the feeding of sodium salts did not produce symptoms of toxemia.

Time does not permit me to continue with an extended description of the various disturbances of the reproductive function resulting from diets inadequate or deficient in various essential foods, minerals, and vitamins. I have already mentioned many of these nutritional diseases and complications. Perhaps the most notable reports of historical significance in the field of nutrition as related to reproduction have been the work of Warkany and others on the effect of various maternal and sometimes paternal nutritional deficiencies on the fetus of the rat and larger mammals, varying from resorption, stillbirths, and neonatal deaths, to bony malformations. Paralleling this work on rats, Burke found an amazingly large percentage of inadequate prenatal diets among the mothers of more than 200 infants, including stillborn infants, neonatal deaths, premature and functionally immature infants, and those with marked congenital defects. These and other research work demonstrate that adequate nutrition for women during pregnancy is an important factor in lowering the incidence of stillbirths and neonatal deaths.

In conclusion, I wish to repeat Burke's statement that there can be little doubt that adequate nutrition of the pregnant woman is sufficiently important to the normal growth and development of the fetus and the health of the mother to warrant a place in all prenatal care programs. "If a good diet is a safety factor to the mother in the prevention of certain forms of toxemia, that alone is important."

In this brief review of certain historical references and the present-day status of nutrition and reproduction, I have departed from the usual philosophical address given by presidents of this body. We have traveled through many centuries to learn something of the fancies and fallacies and, finally, of the present-day facts of nutrition and its possible relationship to human reproduction.

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# MEDICINE'S RESPONSE TO THE CHALLENGE OF OUR TIME*

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DRAMATIC indeed have been recent accomplishments in the specialties of obstetrics and gynecology. There has been a gratifying decrease in the maternal death rate largely due, perhaps, to better prenatal care, conservative obstetric procedures, and the advent of chemotherapy and antibiotic treatment generally. Since my days of practice one of the most interesting developments is the discovery of the Rh factor in blood compatibility and the application of this knowledge in blood transfusions and in an understanding of the pathogenesis of fetal erythroblastosis. Investigations of dietary deficiencies which have been carried on for many years are finding new applications. This is true also, I am told, of complications of pregnancy such as anemias and toxemias and in the correction of mineral and vitamin deficiencies affecting the mother and the fetus. In the field of gynecological surgery, we note the description of new surgical techniques in general and cesarean sections in particular. Renewed interest in such procedures as the Wertheim operation for cancer of the uterine corpus indicates that definite progress is being made. Progress in cancer studies generally is accelerating and a better understanding of this histochemical process is coming to light which will benefit mankind through the clinical specialties.

As the problems of medicine are pursued to their fundamentals, it is interesting to observe that they are all grounded in the natural sciences as they apply to the life process. It is on this firm base of scientific knowledge that all our medical specialties rest. Our specialties of medicine, for a time somewhat isolated from one another, are gradually drawing closer together. This process has been speeded as we have increased our knowledge of the inter-relations between various parts of the body.

It is encouraging indeed to note the renewed emphasis your specialties place on the importance of research in education and training.

It is sometimes difficult to see the full drama of the development of modern medicine in the perspective of history. We should remember that only some forty generations of fifty years each have elapsed since Hippocrates lived and only two or three since the development of modern medicine as we know it began to take form. Only in the twentieth century, for instance, has medical science been able to minimize the ravages of war by reducing the morbidity of epidemic disease and nonbattle casualties below that of battle casualties. During World War II important advances were made in the cure of battle casualties as well.

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As a result of tremendous advances in the study of the life process through the tools of chemistry, physics, and physiology, we have learned to conceive of man as an animal organism constantly interacting with his physical environment, striving to maintain a harmonious balance of physiological and chemical activity. At the same time we have learned that he is a social organism as well, constantly interacting with other units of the social system of which he is a part. We know also that the momentum of technological change has increased tremendously during the past century, in medicine as in other areas of our society. It is not strange that, in the social process of adaptation to meet revolutionary changes in the production and distribution of goods and in communication and transportation, we are faced with recurring economic and social crises. Only to the extent that society can adapt itself to the constantly changing demands of our technological age will it be reasonable to expect all men to find a degree of happiness.

Increasingly, medicine is focusing its attention on man as a social organism. The realization is growing that, while there are volumes yet to be learned about the physical aspects of man in health and in disease, the great contributions of the future will spring from an understanding of those subtle functions and forces which determine man's reaction as an individual in a social organization. Justice Holmes put it more succinctly when he wrote: "Man, whether he realizes it or not, is always fighting for the kind of a world he wants." The challenge of the future lies in man's constant struggle, consciously and unconsciously, to find happiness in a changing world, a world that is constantly making new and greater demands on both society and on the individual. This challege goes very deep indeed to the very roots of the problem of man's survival on earth. Medicine is concerned with the preservation of life, with man's survival in this complex and ever-changing world. Perhaps no other group of professional men is more concerned with this whole problem than this Association.

As I have suggested, we are increasingly interested in the social aspects of life and living. Our primary concern always has been and always will be the individual and his health. But today the individual human being is caught up in forces far beyond his own personal control. Perhaps the most important single fact with which all of us are faced—particularly American leaders in the professions, in business, and in government—is the stark fact that the world's population is increasing faster than man's capacity to supply all his basic needs. Despite the loss of millions of people directly and indirectly because of the war, the world's population has continued to increase to a present total of approximately two billion, one hundred fifty million people. At the time of the American Revolution the population of the world totalled some six hundred thirty million, less than a third of the present figure. In our own country the population has almost doubled since 1900, increasing from seventy-five million to approximately one hundred forty-four million people. Increasing attention is and must be given to the problem of making the resources of the earth provide means of subsistence for this ever-growing population. It has been taken for

granted that the resources of the earth are limitless, and that they can endlessly supply the needs of an ever-growing world population. Serious studies have shown, however, that the material resources of the earth have been seriously depleted in many areas. Such a depletion of resources has spelled the end of civilizations of the past.

Physicians always have known that man is part of his physical environment, that he definitely depends upon it for his survival, and that he is equally dependent upon his fellow human beings in a society of which all men are essential elements. Concerned as we are with the welfare of the individual man and woman, we must also do our part as medical men in solving the problem of mankind's adjustment to its environment and to the resources of the earth. Only in our generation have science and technology begun to address themselves to the problems created by man's impoverishment and looting of the earth.

We have learned painfully, for example, that to mine the hills of their forests without making provision for their replacement not only robs us of a resource but also creates abnormal conditions which lead to floods and destruction. The science of forestry is teaching a new program of perpetual yield of timber crops which preserves not only timber but the soils and their wealth as well. Likewise, agriculture is preserving the wealth of the soil through better planned farming which will give a perpetual yield of crops.

Whether man can correct the damage already done to his material means of subsistence in time to stay the deterioration of present world civilization is one of the real crises of our times. The solution of this problem is basic to the whole problem of war and peace today, tomorrow, and next year, and in generations to come. As Americans, we are particularly fortunate because of the great, though not unlimited, resources of our nation. Compared with other parts of the world, ours is abundance indeed, but we cannot ignore the basic problems faced by mankind elsewhere. We have learned at great cost that this is one world or it is none, even though we know painfully that today we live in two worlds not of our choosing. We know that the world will one day be united again, either by peaceful or by warlike means. The basic problem, however, will still remain: that is, how man can harmoniously adjust himself to the world in which he finds himself and to its resources for supporting him?

What will be man's response to his responsibility for the future of mankind?

I suggest that medicine's response to the challenge of our times is a vital and most important one. Fundamentally, medicine is concerned with the preservation and nurture of mankind. While we must continue to serve individual human beings with all our knowledge and our skill, more than this we must, along with other leaders of our communities, join in every serious effort to make a more satisfactory adjustment of man to his world. This involves such practical pursuits as aiding in all conservation programs, supporting educational and research activities which will provide the know-how and the skilled personnel in scientific and technological fields necessary to conserve and develop the resources of depleted parts of the earth.

Planned parenthood, as a partial answer to this problem, will naturally command our special interest. We have a special obligation, I think, to encourage educational opportunities for millions of underprivileged people and thus aid in controlling population growth where it needs control. The United Nations, UNESCO, and the World Health Organization offer the possibility of developing world-wide programs along these lines that can materially affect the course of contemporary civilization. All that has been accomplished since the war in bringing relief and reconstruction to war-torn countries is a mere buying of time in which to solve the greater problem of the total adjustment of mankind to his total physical and social world.

Economic and political systems which help to alleviate the acute symptoms of the day will not cure the chronic social and economic disorders that have grown out of man's quest for the means of survival. Most of the wars of history have arisen from the basic needs of people for expanded land areas for the production of food, fiber, and shelter. The wars of this century have risen to cataclysmic force. In another war, our population problem may be solved simply and in a relatively short time. Whether the survivors can make any kind of satisfactory adjustment to their earth is something no one can predict. But, through modern science and technology, the intelligent use of all media of communication, by education, by good will and cooperation, man can, if he will, arrest the downward spiral of our civilization. This task places great responsibility upon the American medical profession, holding leadership as it does among the medical professions of all nations and dedicated as it is to the health and welfare of mankind. Ours must be a response that will aid all men of good will to seek solutions to the major problems of survival which face mankind.

Is this not the crisis and struggle of our time? Are there not too many people who have little or no respect for their fellow men—too many people who seek only to gratify their own selfish and acquisitive instincts? What a tragedy this is when probably, surely, there is enough for everyone's need but, as someone recently remarked, not enough for everyone's greed. The physician, like the philosopher and the saint, puts down this sorry scheme of things as man's baser nature and, with patience, kindliness, and tolerance, goes about his work of healing and prays that time will not run out. As we look back across the years of man's struggle and despair and forward to the better times we may have if we but will, we must see to it that, centuries from now, men will look back and say of us that we built upon the best that was in us and fashioned a better world for them. Medicine, with its age-old concern for the sick, the poor as well as the rich, the weak as well as the strong, has been an influence for good surpassed only by the moral precepts of religion. The services of medicine, like those of religion, have been largely personal. Medicine of the future must progress as a social, as well as biological, science and must broaden its outlook accordingly. Medicine is coming of age as a social science in the service of mankind and of his society. This must be medicine's response to the challenge of our times.

# A SURVEY OF 113 CASES OF PRIMARY DYSMENORRHEA TREATED BY NEURECTOMY*

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BEFORE reading the technical part of this communication it is right and proper that I should show full appreciation for your invitation to deliver this Joseph Price Oration. Surely it is unnecessary to labor the fact that such an invitation, which is one of the highest honors that lies within your power to confer upon a colleague, not only does honor to me, personally, but also to Trinity College, Dublin, to the Rotunda Hospital, Dublin, and to the Dublin School of Medicine. I fully appreciate the high opinion you, in this great Country, hold of Irish obstetrics, and especially of that pioneer maternity hospital of which I am proud to say I am the present Master.

Although now chiefly concerned with obstetrics, I have been keenly interested for many years in the problem of dysmenorrhea and, without wishing to advertise the fact that I have written and worked considerably upon this subject, I cannot avoid referring occasionally throughout the text to my own publications.

I flatter myself that some points I have noted are advances in our knowledge, and it is for this reason that I put some facts and figures before you. I do not flatly contradict time-honored concepts, but I am convinced that many cases of primary dysmenorrhea are wrongly treated because of faulty diagnosis. Nor do I pretend to be able to explain with certainty why dysmenorrhea occurs—in other words, I am at a loss as to its exact etiology—but I am sure that in primary dysmenorrhea there are definite nerve lesions in the presacral, the ovarian, or both systems, and that menstrual pain usually can be relieved by appropriate and thorough nerve division.

I hope to be able to convince you that it is possible to differentiate between menstrual pain of ovarian or uterine origin, and also to show that dysmenorrhea may be a mixture of both. I also hope to clarify and dispel some doubts which exist regarding the harmful effects of nerve section upon the female genital organs, their fertility, and their reproductive powers. The cases under review were operated upon sufficiently long ago to enable me to assess the results confidently, and it is my belief that neither ovarian nor uterine denervation, nor combined ovarian and uterine denervation, assert a harmful effect upon a woman's vital functions. What follows has been most

*The Joseph Price Oration for 1948, delivered at the Fifty-Ninth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 9 to 11, 1948.

carefully considered, and I hope it will both carry weight and invite verification. May I say that, in order to exclude any personal favor, the results have been assessed and tabulated by an independent observer. With few exceptions the operations were performed in Sir Patrick Dun's Hospital, Dublin, where I was Gynaecologist for twelve years prior to my appointment to the Rotunda.

## The Material Under Review

The clinical material upon which this paper is based concerns 113 young, and otherwise healthy, women whose dysmenorrhea was considered *primary* and to be so severe that they were unable to live normal lives, being incapacitated to a serious degree each month. The review covers the years 1936 to 1945, and in 1945 the 113 women who had been treated by some form of nerve division were written to in order to "follow up" the results. No contact was established with 31, but there were 82 replies. Unfortunately, the details of a further 24 cases were lost and these are not included.

I will now consider the 82 cases of dysmenorrhea from which replies were received. The treatment was as follows:

21 Ovarian denervations.
34 Presacral sympathectomies.
27 Combined ovarian and uterine denervations.

It is first necessary to state the criteria from which I believe it possible to make a differential diagnosis of the source of primary dysmenorrhea.

## The Differential Diagnosis of Ovarian From Uterine Pain

The most obvious method of discovering if the menstrual pain is of ovarian origin is to apply reasonably firm bimanual compression to the ovary while asking if the pain or discomfort thus produced is similar to that experienced at the menstrual times (the viscero-sensory reflex). If so, this would be a reasonable indication of the origin of the pain, of the discomfort, and of the nausea. But in many the discomfort thus produced does not resemble the menstrual pain, and it is then possibly of uterine origin. The "sound test" I have already described elsewhere is of the utmost importance in establishing a correct diagnosis.

*The Sound Test.*—The passing of a sterile uterine sound, either by touch or by sight, is usually easy and, in my experience, has never been followed by immediate or remote ill effects. All precautions should be taken to exclude pregnancy, cervical infection, or other contraindication, before the sound is passed. In several of my early cases a small intrauterine bag was inserted into the uterus, with full aseptic precautions, and was inflated to 5 c.c. capacity, to test for uterine pain. In others, when the Fallopian tubes were blocked, Rubin's apparatus was used *without* anesthesia, up to 300 mm. Hg pressure. The intrauterine bag has obvious disadvantages, and it was not used lately.

These methods of investigation yielded peculiarly uniform results, and while typical uterine pain is accurately referred to the immediate suprapubic area in the midline of the lower abdomen, it sometimes reached as high as the umbilicus. This was true in 49 per cent of the patients examined. In 11 per cent of somewhat exceptional instances of primary uterine dysmenorrhea the passing of the uterine sound produced typical referred pain in some other

lower abdominal area. In most of these girls there was some palpable pelvic abnormality (*secondary* dysmenorrhea); the consideration of these is outside the scope of this paper, but undoubtedly the associated pathological conditions are responsible for the abnormal pain distribution.

The passing of the sound was absolutely painless in approximately 36 per cent of patients, many of whom did not suffer from dysmenorrhea; it produced pain referred exactly to the umbilicus in 2 per cent, and to the midline of the vulva about the position of the clitoris in the other 2 per cent. From these data we can separate with some accuracy the cases of true uterine pain from those of ovarian origin, and likewise interpret correctly co-existent mixed ovarian and uterine symptoms.

True primary ovarian pain is referred with equal frequency to either side of the lower abdomen, but diffuse lower abdominal pain probably indicates mixed dysmenorrhea of both uterine and ovarian origin. Ovarian pain itself appears typically in the two or three premenstrual days, rarely persists after the onset of the flow, and sometimes disappears before bleeding begins. In contrast, although uterine pain may be occasionally premenstrual in onset, it usually begins with the flow, ceasing after an hour or two, or persisting until the bleeding has completely ended. Ovarian pain is nauseating in character, being of a continuous dull, dragging type, and is probably similar to that evoked in the male as a result of trauma to the testis. Ovarian pain can be faithfully reproduced by evoking the "deep sensibility reflex" of the ovary by pressure upon one or both ovaries during bimanual examination, and radiation down the thighs (the viscero-sensory reflex) often can be produced in this way. Only occasionally is uterine pain evident as a dull ache; in dysmenorrhea it varies typically in intensity being subject to exacerbations and is frequently sharp, stabbing, cramplike or colicky in character.

In brief, ovarian pain may be uni- or bilateral; menstrual but chiefly premenstrual; always subumbilical, but chiefly left-sided and radiating down the thighs. Although not included above, nausea is an almost constant symptom, whilst dyspareunia, dyschezia, and syncope are frequently present.

It should be comparatively easy, therefore, to separate the various types of primary dysmenorrhea from one another and to apply more specific treatment for their relief. Hormonal treatment, cervical dilatation, uterine curettage, and all other measures directed toward the relief of supposed uterine spasm, should be reserved for appropriate cases.

It may have no bearing upon the etiology or treatment of primary dysmenorrhea but the following interesting facts emerge from analysis of Tables I, II, and III.*

| | ONSET OF PAIN | AGE AT OPERATION |
|---|---|---|
| Primary uterine dysmenorrhea | 20.8 years | 24.2 years |
| Primary ovarian dysmenorrhea | 18.5 years | 23.7 years |
| Primary combined dysmenorrhea | 19.7 years | 23.2 years |

From this, it seems that most cases of intolerable menstrual pain reach a climax between 23 and 24 years of age, but that pain of primary ovarian origin has an earlier onset than that of primary uterine pain. It is only to be expected that menstrual pain of mixed origin would manifest itself midway between both varieties.

*Lesions and Abnormalities of the Painful Ovary.*—For the purpose of this discussion I will consider the painful or tender (though apparently normal) ovary, and exclude the frankly diseased, adherent, inflamed, or enlarged or-

*Tables not published.

gan, as found typically in *secondary* dysmenorrhea. My remarks will be thus confined to the cases which must be regarded as true *primary* ovarian dysmenorrhea. These constitute a certain proportion of our difficult cases; the grossly diseased ovary is readily recognized and accepted as a source of pain, but such pathology is unusual in the young patient in whom the typical symptoms of primary dysmenorrhea exist.

Sclerocystic changes in the ovary are of the greatest importance in ovarian dysmenorrhea, and were present in all my own cases, but some writers maintain that the small cirrhotic ovary with its thickened white capsule is an equally important etiological factor. L'Hermitte, and others of the French School, support the neurogenic etiological theory, and believe that ovarian sclerocystic changes are secondary to the influence of some ovarian nerve lesion rather than a primary condition. They regard cyst resection, or any other operation productive of ovarian scarring, as ill-advised and favoring recurrence of the symptoms by producing further cicatrization with fibrosis and pressure on the nerve endings. To support this there is very definite evidence of a peri- and intrafascicular ovarian nerve degeneration in such cases; some regard this as constant findings in ovarian sclerocystic disease, and similar degenerations are frequently found in about 70 per cent of the presacral nerves in intractable uterine dysmenorrhea.

I can confirm these findings relative to the presacral and ovarian nerve lesions in such cases, and it is interesting that none of these changes were found in the ovarian nerves examined from women who had not suffered from dysmenorrhea (i.e., the "controls") and for whom hysterectomy was performed for some uterine disease. Further "controls" within the dysmenorrhea age were also obtained when it was established that ovarian denervation did no harm to function.

If we accept the neurogenic theory of sclerocystic ovarian degeneration, and the association of pain with coincident ovarian nerve lesions, we can readily understand that only certain ovaries will be painful, and why it is that pain is an unusual symptom in the many and various sized ovarian cysts encountered. It also becomes apparent how "Mittelschmerz" may be totally absent in most women, but present or excessive in the minority whose ovarian nerves are abnormal. The two determining factors productive of excessive ovarian pain appear to be an existing nerve degeneration with pressure upon either the ovarian intrinsic nerves or some fibrils adjacent to the granulosa cell layer of a follicle. Such pressure could be continuous (from excessive fibrosis in the proximity of nerve endings) or periodic (from the edema present at the time of ovulation and in the premenstrual phase).

The question of pressure upon the fibrous or inflammatory nodules described by Neuman, and such nodules are now known to exist on the ovarian terminal nerve filaments in close relation to the ripening Graafian follicles, is particularly interesting. These nodules are most numerous in the prepubertal and postmenopausal ovary, being almost entirely absent around the follicles of the actively menstruating and multiparous woman. Their exact significance is unknown, but their frequent presence in those patients who are most liable to suffer from severe dysmenorrhea lends support to the neurogenic etiological theory.

The accepted ovarian lesions of *secondary* ovarian dysmenorrhea, e.g., a prolapsed and grossly cystic ovary, a small ovarian endometrioma or abscess, oophoritis, ovarian apoplexy, light pelvic adhesions, ovarian varicocele, parovarian tumors, are outside our present consideration. Celibacy, masturbation, or too frequent coitus, were believed by Ashton to cause ovarian con-

gestion and resulting pain. They are, admittedly, possible factors in the production of dysmenorrhea, especially when a nerve lesion is present, and are often noted in case histories of patients suffering from dysmenorrhea, but Ashton's view has not received much support.

*The Ovarian Nerve Supply (Intrinsic and Extrinsic).*—To agree that ovarian dysmenorrhea can exist, either as an entity or in conjunction with menstrual pain of uterine origin, implies acceptance of the view that the two structures possess their own independent and separate nerve supplies. This is now known to be true. Learmonth, Mitchell, and other histopathologists still doubt the possibility of a direct anatomical connection between the tubal and ovarian nerve supplies, but the absolute independence of the uterine and ovarian systems is generally accepted. *Ovarian innervation is bilateral, and pain originating in one ovary may be referred either to that side or to the opposite side, or to both the affected and the normal sides.* The clinical importance of this fact is readily appreciated.

The ovarian nerve supply is chiefly sympathetic, being derived from the renal, intermesenteric, and celiac plexuses. The ovarian nerves enter the hilum of the ovary in two or three main trunks, and then split up within the substance of the organ to accompany the arterial ramifications and end outside the theca externa of the follicle. Any statements that the terminal nerve fibers penetrate the membrane granulosa have been disproved, but they form an extremely dense network around the follicle and are intimately connected with it. It is just possible that a few fine, terminal twigs may leave the ovary between the layers of the mesolapinx to end near the Fallopian tube and uterine cornu, but their final destination is unknown.

The vascular state of the ovary is controlled by the (dilator) impulses of the few parasympathetic fibers in antagonism to the richer sympathetic (vasoconstrictor) supply. In an organ subject to cyclic variations this is undoubtedly of importance in the control of the degree of congestion and the possible production of pain. Consider what the male would experience were the processes of ovulation to take place monthly in the testes.

With reference to the possibility of harm being done to the ovary by surgical denervation, it is well to remember that the stabilization of vascular tone within an organ thus suddenly deprived of its control is known to be rapid and without ill effect, even when the organ in question is functionally dependent upon its nerve control. The ovarian function and cycle are uder *hormonal* control, and both are unimpaired by nerve section except that pain impulses cannot subsequently spread thence to the higher centers.

Pathways for painful ovarian stimuli exist in the ovarian nerves, as is known to be so in the presacral system in connection with the uterus, and the success of ovarian denervation depends upon this.

## The Treatment of Ovarian Dysmenorrhea

In 1929 L'Hermitte and Dupont and, independently, Leriche suggested that a painful ovary could be rendered insensitive by denervation. They knew that Cotte's operation was proving successful in carefully selected cases of presacral sympathectomy and believed that a similar ovarian denervation should give satisfactory results. The report of their early work proved interesting for they soon realized that, owing to the nerve cross link between the ovaries, successful denervation was necessarily bilateral. They also found that a uterine suspension operation improved the results when retroversion was present, as did appendicectomy when there was evidence of appendicitis.

Their most recent technique was, in brief, the division of the two or three main ovarian nerve bundles in the mesovarium without interference with the ovarian blood vessels.

Independently, and without knowledge of their work, I carried out the same operation by a simplified technique on several patients, with most encouraging results. The failures were due to my then inability to separate the uterine from the ovarian cases, for what I describe as distinctive signs and symptoms of ovarian, uterine, and mixed dysmenorrhea followed later.

My technique for ovarian denervation still consists of simple division of both infundibulopelvic ligaments, their nerves and blood vessels, and simple ligature of the stumps with catgut. To avoid the possibility of elongation of the divided ligament with subsequent prolapse of the ovaries, the cut ends are sutured carefully to one another and, where necessary, ovarian and uterine suspension has been performed. Appendicectomy, when indicated, has been a routine procedure. My bilateral denervations have been most encouraging—the earlier cases of unilateral division were disappointing. This has already been referred to, and is probably due to the close crosslinkage nerve supply of the ovaries.

## Ovarian Denervation

The twenty-one cases of primary dysmenorrhea treated by ovarian denervation alone (i.e., cases diagnosed as purely primary ovarian dysmenorrhea) gave the following results over the period mentioned:

| | |
|---|---|
| 3 failures | 14.2 per cent |
| 1 partial success | 4.7 per cent |
| 17 successes | 80.9 per cent |

## Presacral Sympathectomy

Thirty-four cases of severe primary dysmenorrhea were regarded as being of essentially uterine origin and were treated by presacral sympathectomy. In some additional operative procedures were used, as appeared appropriate. The results of the presacral sympathectomy operations in these 34 cases were as follows:

| | |
|---|---|
| 4 failures | 11.7 per cent |
| 5 partial successes | 14.7 per cent |
| 25 successes | 73.5 per cent |

*The Presacral Nerve.*—The so-called presacral nerve is singularly accessible to the operator in its retroperitoneal position in front of the last two lumbar vertebrae within the space bounded laterally by the two common iliac arteries. The presacral nerve is usually a well-defined fine plexus (the superior hypogastric plexus) rather than a single, large trunk, and in only 3 per cent was its free exposure made difficult by the proximity of the pelvic mesocolon.

The presacral nerve contains sympathetic and parasympathetic elements, and its continuation through the middle and inferior hypogastric plexuses on the front of the sacrum finally links it with the nervi erigentes. From this plexus thus formed the nerve filaments and ganglia are distributed to the uterus closely following the main arterial supply. Eventually the intrinsic uterine innervation ends subperitoneally and beneath its endometrial lining; there is no evidence of penetration of the uterine lining by nerves, nor are ganglia common in the uterine muscular tissue.

*Operative Technique (Presacral Sympathectomy).*—I have no special technique in performing presacral sympathectomy. This operation has been ade-

quately described by others, and each operator develops his own particular system. I am satisfied, however, that incomplete presacral neurectomy and incorrect diagnosis are the commonest causes of failure. It is also important to remove at least one inch of the individual nerve fibers or of the plexus itself. If this is not done re-establishment of nerve continuity may lead to recurrence of the pain.

### Combined Ovarian and Uterine Dysmenorrhea

From the 82 cases of severe dysmenorrhea treated by nerve resection, 27 appeared to be of mixed ovarian and uterine origin. In these cases presacral sympathectomy was combined with bilateral ovarian denervation with the following results:

| | |
|---|---|
| 1 failure | 3.7 per cent |
| 4 partial successes | 14.8 per cent |
| 22 successes | 82.2 per cent |

### The Nerve Findings and Histopathological Studies

Analyzing the specimens which have been examined, 49 were from the hypogastric (presacral) nerves, and 27 from the nerves of the infundibulopelvic ligaments. A total of 76 microscopical sections were examined and, as there was no gross variation in the sections obtained from either group, the following description will suffice for both. Many more sections than the number quoted were examined, but my collaborator, Dr. David S. Torrens, Professor of Physiology, Trinity College, Dublin, was unable to devote the necessary time to detailed records of all the cases.

The fixative generally used was Heidenhain's mercuric chloride salt solution ("Susa"), and paraffin sections were made in all cases. Mallory's connective tissue stain was found to be the most useful, and this and polychrome methylene blue were employed as a routine. We (O'D. B. and D. S. T.) have studied:

1. The normal tissues.
2. The changes in the nerve trunks.
3. The changes in the small ganglia which are commonly found in the hypogastric nerves.

1. *The Normal Tissues.*—Specimens of the hypogastric (i.e., the so-called presacral nerves) usually contain numerous well-defined bundles of nerve fibers. Some of these included only ten or twenty fibers, while others are much larger. Both myelinated and nonmyelinated fibers are present. Most of the myelinated fibers are small, but there are also some large fibers. The nerves are embedded in fibrous tissue, which also contains numerous blood vessels and varying amounts of plain muscle. The tissue from the infundibulopelvic ligaments is similar, but nerve bundles are fewer and, as a rule, smaller. Groups of ganglion cells lie here and there among the fibers of the hypogastric nerves, but are seldom present in the ovarian nerves. The nerve fibers in the infundibulopelvic ligaments are chiefly postganglionic. Large cells of chromaffin type may sometimes be found among them; they resemble the chromaffin cells often found about the hilum of the ovary and should not be mistaken for ganglion cells. Lymphoid tissue is frequently present among the hypogastric nerves. The general structure of the ovarian and hypogastric nerves is similar to that of autonomic nerves in other parts of the body. There is the usual variable, but quite small, amount of fibrous tissue in the nerve trunks between the nerve fibers; this forms an endoneurium.

The ganglion cells in normal specimens have the usual appearances of healthy autonomic ganglion cells, varying in size and shape, and filled with well-defined Nissl granules. The capsule of "satellite" cells, described by Davis and others, is seldom recognizable and the arrangement is, perhaps, more characteristic of cerebrospinal than of autonomic ganglia. As the silver techniques were not used it was not possible to distinguish certain features mentioned by Davis, such as the various cell types of Cajal.

2. *Changes in the Nerve Trunks.*—In what we regard as abnormal specimens there is a marked increase in the amount of intraneural fibrous tissue. In the normal nreves, carefully stained by Mallory's method, the fine collagen fibrils of the endometrium can be clearly seen; in abnormal specimens the endoneurial tissue, besides being greatly increased in amount, often appears structureless and hyaline. In many specimens some of the nerves seem to be quite normal; in other nerves from the same specimen there is extensive involvement. The gross inflammatory changes described by Davis, such as infiltration of the nerves with polymorphonuclear cells, lymphocytes, and plasma cells, microscopic abscess formation, etc., have not yet been observed in our cases; nor have we found the advanced arteriosclerotic changes he describes.

Identical changes have been repeatedly observed in the ovarian and presacral nerves, and it is believed that a similar process may affect either, or both, systems. In addition to an intraneural fibrosis, a perineural fibrosis is present in a small proportion of cases; this, however, appears to be the exception rather than the rule.

3. *Changes in the Ganglia.*—These are commonly more marked than the changes in the nerve trunks. In abnormal specimens there is a definite increase in the number of small cells in the tissue between the ganglion cells. Whether this increased population is due to proliferation of local "satellite" and other cells, or to immigration of cells from other places (e.g., from the lymph nodes frequently present), or to both causes, is unknown. Some of the small cells may be lymphocytes or plasma cells, but many of them appear to resemble microglia or "Hortega cells." In addition to these small cells, large wandering cells resembling "mast cells" are frequently present in small numbers in the ganglia, but less frequently in the nerve trunks.

Many of the small cells under consideration are found clustered around and upon the bodies of the ganglion cells, and actual phagocytosis of the ganglion cells (neuronophagia) is common. The ganglion cells also show degenerative changes, pigmentation, chromatolysis, and disintegration, and here we are able to confirm the observations of Davis. We suggest that the ganglion cell may be the primary focus of an attack by the unknown causal agent, for in several specimens the ganglia are affected while the nerve trunks appear normal. Conversely, in specimens where the nerve trunks show definite fibrosis, the ganglia are always seriously involved, and many of the cells damaged and destroyed. The changes we have constantly observed may be summarized as:

1. Degeneration and destruction of sympathetic ganglion cells.
2. Degeneration of postganglionic fibers.
3. Replacement fibrosis in the nerves.

There are, clearly, two questions which require consideration:

1. What is the cause of the changes in the nerves?
2. What is the relation, if any, between the nerve changes and dysmenorrhea?

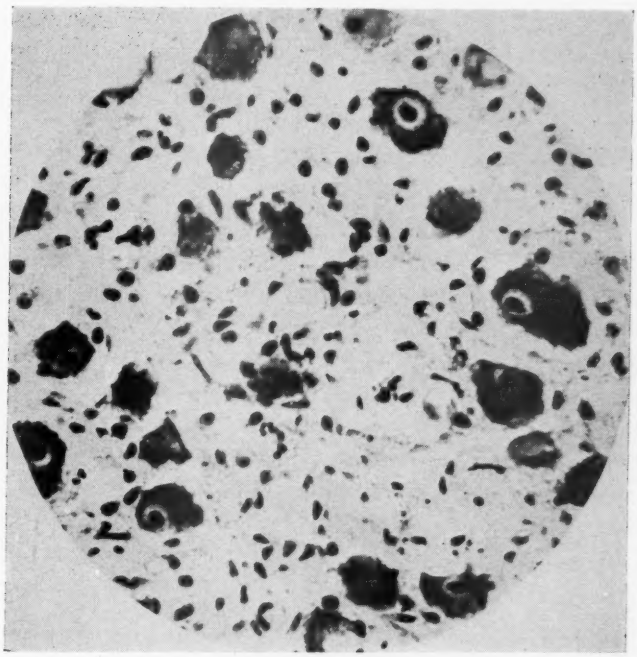

Fig. 1.—Ganglion cells from Case K. R. 9. Regarded as normal. Healthy cells with typical Nissl granules and with very few "satellites." No appearance of infiltration with other types of cell.

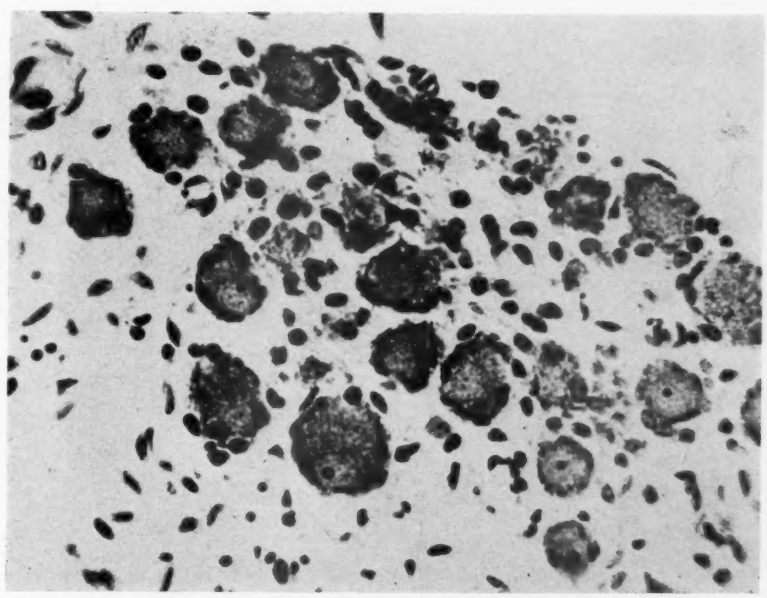

Fig. 2.—Ganglion cells from Case A. H. 1. Regarded as abnormal. The cells show some chromatolysis, and there is a definite increase in the number of small cells possibly of microglial type. Many of these are concentrated about and upon the ganglion cells, and there are indications of some neuronophagia.

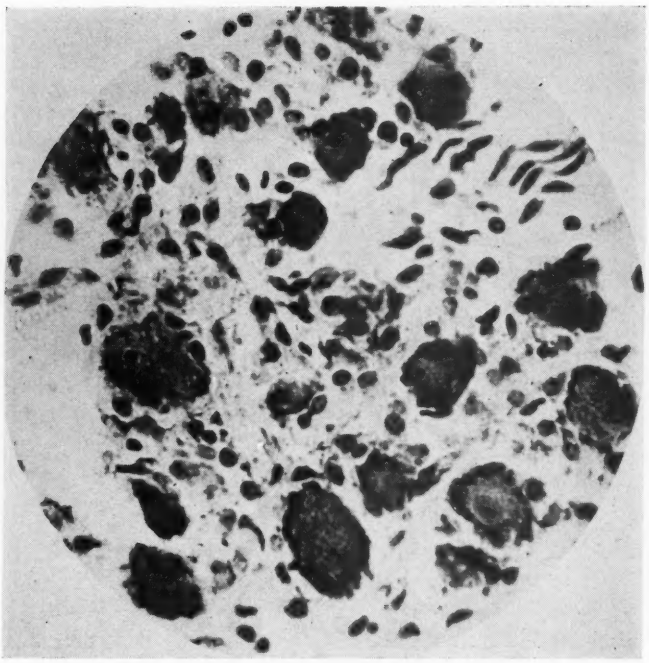

Fig. 3.—Ganglion cells from Case B. F. 11. Regarded as abnormal. The condition is very much the same as that seen in Fig. 2.

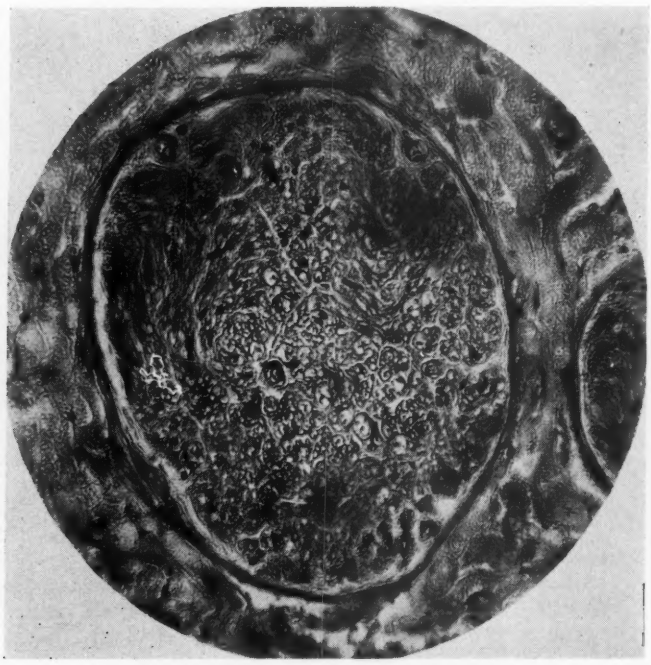

Fig. 4.—Nerve trunk (presacral) from Case K. R. 9. Regarded as normal. Shows myelinated and nonmyelinated fibers. Note relatively small amount of endoneurial fibrous tissue.

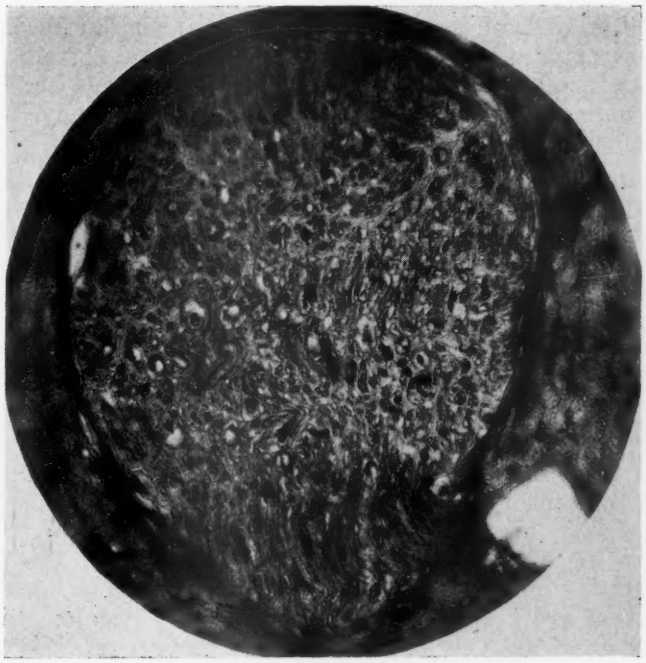

Fig. 5.—Nerve trunk (presacral) from Case B. H. 13. Regarded as abnormal. The endoneurial fibrous tissue is increased and many nerve fibers are almost obliterated.

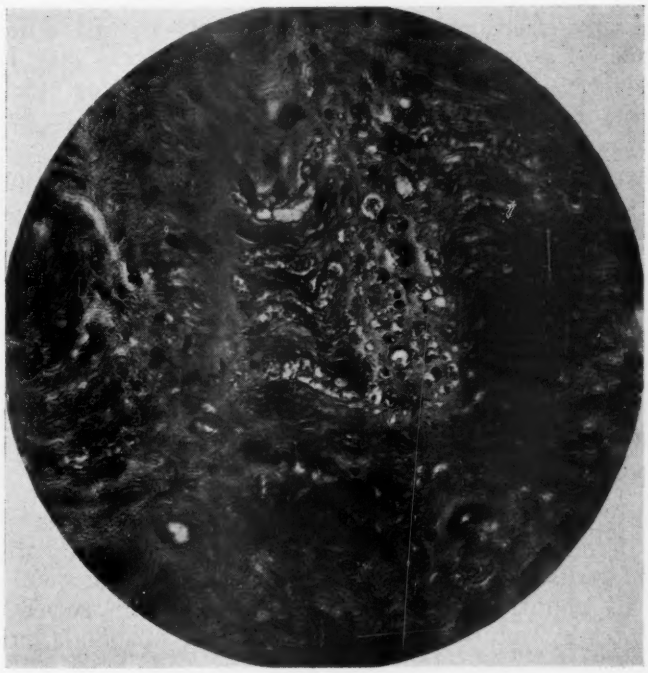

Fig. 6.—Nerve trunk (presacral) from Case B. F. 11. Regarded as abnormal. The endoneurial fibrous tissue is increased and shows what appears to be hyaline change.

Neither question can yet be answered with certainty. The appearances seen in the nerves of both systems are somewhat similar to those found in cerebrospinal nerves and the root ganglia in zoster and certain types of toxic neuritis, such as arsenical neuritis. Comparable changes are also found in the nerves in animals suffering from vitamin $B_1$ deficiency, and in human beings with beriberi.

The relation of the nerve changes to pelvic pain is also far from clear, but certain facts may be indicated. The hypogastric and ovarian nerves contain not only the sympathetic afferent supply to the pelvic viscera, but also sensory afferent fibers from these organs. We believe that the afferent nerves are first attacked, some of the ganglion cells becoming involved, and that their axons, the postganglionic fibers, consequently degenerate. It seems probable that the sensory fibers are secondarily implicated, possibly as a result of the fibrosis. The pain of dysmenorrhea clearly is not due to direct involvement of the sensory fibers, for if so it would be constant and continuous, and not specially related to the menstrual cycle.

It appears probable, therefore, that the sensibility of the fibers may be altered so that the sensory impulses from the uterus or ovary, which normally do not produce pain, become painful. It has been shown by others that attacks of severe menstrual pain generally coincide with the uterine movements. The uterine movements, normally painless, thus become painful if the sensory nerves are hypersensitive. In contrast, dysmenorrhea of ovarian origin is chiefly or exclusively premenstrual in occurrence, and coincides with the congestion and increased tension in the ovary at this phase.

A further possibility is that, in the early stages of attack and before the ganglion cells are destroyed, the causal agent may produce irritation and increased activity of the cells. This may lead to an increase of uterine motility, which would reach a climax during the menstrual period and cause visceral pain by the usual means. The vasomotor activity of the nerves may also be of importance. Vasomotor disturbances of the uterus may be a source of pain, but in primary ovarian dysmenorrhea the vasomotor condition is probably the chief factor since muscular action can play little or no part.

## Fertility Subsequent to Any Form of Nerve Resection

In reviewing the 82 cases which replied to my 1945 questionnaire, thirty were either married before operation or married subsequently. Analysis of these potential mothers shows that:

Eighteen produced full-term living children, without undue trouble.

Two miscarried.

Two who had been married only a few months at the time they received my questionnaire could not be regarded as conclusive evidence in reviewing the results.

One unmarried girl had a normal pregnancy and delivery.

Thus, twenty out of a possible thirty married women showed a high rate of fertility, a percentage parturition rate of 66.6 per cent, which compares favorably with statistics from a cross section of the normal adult female population in my country. No effort was made in this series to correct the final fertility rates by detailed investigation of the husbands but, presumably, any lack of fertility would be subject to an average male infertility rate of 25 per cent. If we accept this it would be fair to add a further 25 per cent to the figure of 66.6 per cent. This leads us to believe that the operations of

presacral neurectomy and bilateral ovarian denervation do not endanger fertility.

The two patients too recently married to be included in this summary probably would have added support to this statement, and we can quote the one further case where an unmarried girl was delivered of a healthy child subsequent to operation.

My experience also shows that labor following any form of nerve resection was neither abnormal, nor easier, nor more difficult than the average. In no instance was there any evidence of either bladder of bowel disturbance.

### The Association of Failure of Relief With the Nerve Findings of Microscopical Sections

There were three failures (14.2 per cent) and the twenty-one cases treated by bilateral ovarian denervation alone. Unfortunately, no nerve sections are available in these (some of the notes were mislaid), and no conclusions are possible from microscopical evidence. It is, however, interesting that in one case (No. A.D.) bilateral ovarian denervation failed, but complete relief subsequently followed a second operation, presacral sympathectomy. This further emphasizes that dysmenorrhea can be of either uterine, ovarian or mixed origin, and that usually a clear-cut diagnosis should be possible.

The details of the microscopical sections in the nerves in three of the four cases of failure by presacral sympathectomy alone can be seen in Table II. They are inconclusive, varying degrees of fibrosis being present. In one case (No. E. F.) the presacral neurectomy operation was difficult, and it is probable that the nerve resection was incomplete. The other three cases supply no useful information but, as has already been stressed, incomplete nerve resection and incorrect diagnosis are the probable causes of failure.

From Table III, case No. M. H. was the only failure in the 27 women for whom combined presacral neurectomy and bilateral ovarian denervation were performed. This illustrates that unless our diagnosis is precise it is better to use the combined operation of presacral sympathectomy and bilateral ovarian denervation than to rely solely upon one procedure.

On studying the nerve sections from this case we found there was extensive and advanced fibrosis both in the presacral nerves themselves and in their ganglia, and that the ovarian nerves on one side were also similarly affected. Despite the fact that the operation did not cure this woman's pain she subsequently became pregnant and produced a living child without difficulty. It is at present impossible to correlate nerve degeneration and operative treatments with fertility, but it seems established that nerve division does not impair reproductive function in the female.

### Incidence of the Various Types of Dysmenorrhea

In the cases under review, as judged by the results over a period of years, primary ovarian dysmenorrhea existed as a clinical entity in 21 out of 82 cases, or 25.6 per cent. Primary uterine dysmenorrhea is more frequent (41.4 per cent), and the follow-up on the 27 cases for which both presacral and ovarian denervation were performed suggest that combined ovarian and uterine dysmenorrhea exists in 33 per cent.

When these figures are compared with my original conclusions, as published in 1939, we find that I then believed that ovarian dysmenorrhea alone existed in only 11.9 per cent of all cases of dysmenorrhea, but that it could be present in association with dysmenorrhea of uterine origin. My estimate was, therefore, too low since further time has shown the incidence to be 25.6 per

cent. I was also of the opinion that 25 to 30 per cent of cases of severe dysmenorrhea were of mixed uterine and ovarian origin. The present facts seem to indicate that this incidence of this type is 33 per cent, and that primary uterine dysmenorrhea completes the remaining 41.4 per cent. It must be stressed again that these figures are only relative to primary dysmenorrhea and do not include those in which gross pelvic pathology exists.

### Objections to the Operation of Neurectomy

It is only natural that I should have been criticized from time to time for subjecting young women to what many, chiefly older gynecologists, consider an unjustifiable and unnecessary operation. Many routine operations we perform today would have been considered unnecessary some years ago, but the constantly increasing safety and the lessened discomfort to those upon whom we operate now make our work justifiable for conditions which are not necessarily fatal. A little thought on this subject makes the point quite clear, and I do not regard operative treatment to relieve menstrual pain unjustifiable when other less radical treatments have either failed or are unlikely to succeed. It has been my rule to try less radical treatments before resorting to laparotomy.

It is not uncommon to be asked, either in all seriousness or by way of banter, how many times I have cut or injured the ureter during presacral neurectomy. I am glad to say that this accident has not happened, and there have been no serious postoperative complications. On one occasion it was necessary to reopen the abdomen the evening of operation for postoperative bleeding, which occurred in one of my earliest cases of division of the infundibulopelvic ligaments. The ovarian pedicle is notorious for its tendency to retract when divided, and to shed (or "roll off") its suture. This had happened, but the nature of the complication was suspected and, at laparotomy, nothing more was necessary than to apply a fresh ligature. This was followed by an uncomplicated recovery.

It has already been mentioned in this text that the objections of possible interference with either a woman's fertility or sexual life as a result of nerve section are groundless. I wish to emphasize this, for I feel that I can speak with authority having carefully followed such cases for so many years.

To conclude my comments on the justifiability of abdominal operations for the treatment of dysmenorrhea, may I add that I think it wrong to withhold nerve section if it is likely to afford relief. There is no reason to fear a catastrophe, even if presacral neurectomy is combined with bilateral ovarian denervation. In my series there has been *no* fatality, and the operation is less likely to be followed by postoperative complications than is the simple appendicectomy.

### How Does Nerve Section Relieve Pain?

This is a point about which there has been much discussion, but finality has not yet been reached. It seems logical to conclude that, if the nerves of the various plexuses contain afferent fibers, their division will block pain impulses passing to the higher centers. It follows, therefore, that incomplete nerve section will not relieve pain, and that pain will continue if an incorrect diagnosis has been made and the wrong nerve system divided.

It can be argued that primary uterine dysmenorrhea, as distinct from ovarian pain, may be due to ischemia of the uterine muscle, and that presacral neurectomy abolishes the vasoconstrictor influence. This is a further possible explanation, but it is not one which is generally accepted even if the

hypothesis is correct. The relief of pain thus afforded probably would be transient, for an organ deprived of its nerve blood vessel control stabilizes this of its own accord. Thus, recurrence of pain would be the rule rather than the exception.

Much has also been written about the possible effect of nerve control upon maturation of the follicles within the ovary but, on practical grounds, there is no support for the view that ovarian blood vessel balance is altered considerably following complete division of the nerve supply.

It may be concluded that, while we do not certainly know how pain is relieved following nerve section, the most likely explanation is the break in continuity of afferent nerve fibers.

## Etiology of Dysmenorrhea

While it is quite impossible to devote time to discuss even current theories on the etiology of primary dysmenorrhea, several may be discarded without apology. I again emphasize the confusion existing between primary and secondary dysmenorrhea, and the scant attention devoted to their differential diagnosis.

I am quite satisfied that the old theory of obstruction to menstrual debris, either at the internal os or in the cervical canal, is incorrect. In my experience cervical stenosis is rare, and the truth or otherwise of this statement can be readily proved.

It may be asked why cervical dilatation relieves pain, even without curetting. I am unable to answer this any better than can our textbooks, but it is a pity these authorities do not stress the fact that the relief of primary dysmenorrhea following cervical dilatation rarely lasts longer than six months. When the pain returns there is recourse to a further dilatation, a nerve section, or some other treatment. Too often do we too lightly perform cervical dilatation, hoping for the best while shutting our eyes to the fact that its benefits are but short lived.

It must be remembered that the remarks throughout this text on the diagnosis and treatment of dysmenorrhea are confined to the complaint in its primary form. I have found no form of nerve division helpful when coincident pelvic lesions have been present. A high percentage of my failures have been due to nonrecognition of this, and I stress this fact so that those who may be tempted to test the efficacy of nerve section to relieve dysmenorrhea in general will refrain from doing so should any gross pelvic pathology be present.

You may be sure that I have given very careful thought to this problem, and state confidently that I regard our present classifications of dysmenorrhea as misleading. They are satisfactory for examinations, but get us no nearer to what matters, namely, the certain relief of menstrual pain.

Having spoken so dogmatically about dysmenorrhea it is to be expected that some of you may say, "Well since you pretend to know so much about it, what causes primary dysmenorrhea?" I must answer truthfully, "I do not know," but that does not prevent my having ideas on the subject. Since dysmenorrhea is more prevalent and intense in what we call the more civilized peoples and in the higher social groups than in the lower brackets, it is my belief that our so-called civilization is the root of the evil, and that if our young women led more normal lives fewer would suffer menstrual discomfort. Our religions, our education and upbringing, and convention honored throughout the world for many years have dictated celibacy before marriage—and here civilization is in direct conflict with Nature. It cannot have

been thoughts upon this subject that prompted the great Samuel Johnson to write, "Marriage has many pains, but celibacy has no pleasures," but his words cannot be considered altogether inappropriate. It is undoubtedly a misquotation here, but your own Oliver Wendell Holmes wrote in "The Poet at the Breakfast Table,"

> "When she was a girl (forty summers ago)
> Aunt Tabitha tells me they never did so."

Times have not changed markedly, women probably not at all; dysmenorrhea persists.

While I disagree with the old teaching that a woman who has a baby subsequently enjoys almost complete relief from menstrual pain, I am convinced that were cases of severe dysmenorrhea following parturition thoroughly investigated they would be found to be of *secondary* rather than primary nature. To put the matter concisely—I believe that so long as our present moral code is observed and young women are denied the dictates of nature, so long will dysmenorrhea continue to be a scourge. But from this do not infer that I am asking you to advocate free love; that *might* be an answer, but I do not recommend putting it to the test!

Possibly some of my audience will say, "Many girls have a moral code which fits your theory, yet they suffer dysmenorrhea." I agree; in many instances this is correct, but again I ask you how many of these cases have been intelligently investigated and proved to be examples of *primary* dysmenorrhea? Only too often do these girls develop pelvic lesions from gonorrhea and other infections.

You may ask, "Supposing your theory is correct, and the leading of life in accordance with the individual dictates and urges relieves the pain of primary dysmenorrhea, how does this happen?" Again, I cannot answer you, but nobody can deny that repressions, the absence of repeated pelvic hyperemia such as accompanies satisfactory sexual intercourse, and the dissatisfactions which follow the abstinences enforced on the many by the trend of life and moral code play their parts. In the absence of gross pelvic pathology the occasional pelvic hyperemia of menstrual periods quite understandably produces pain. Were the pelvic organs and their blood and nerve supplies exercised earlier, and more regularly, by free sexual intercourse (and possibly pregnancy) this severe monthly menstrual engorgement pain would fade into insignificance.

We know little, too, about what effect the enormous blood hormone levels associated with pregnancy have upon a woman's genital apparatus. We attribute the softening of the pelvic structures, even that occurring in the ligaments binding the bony pelvis together, to hyperemia. But is this enormous change entirely the result of hyperemia? Surely the hyperemia of pregnancy and the changes in the ligaments, the pelvic fascia, and the uterine supports throughout the genital tract must be largely due to hormone effect.

In concluding these speculations it seems as if we may compare primary dysmenorrhea to a deficiency disease. It may be asked then, "Why is hormonal therapy so disappointing in these cases?" The answer is probably that we little appreciate the enormous dosage required and our estimates are too low.

Before ending I wish to thank Professor David Torrens and his staff, and all my colleagues at Sir Patrick Dun's Hospital, for their encouragement and help. I am especially indebted to my secretary, Miss May Walmsley, for unfailing and helpful enthusiasm in the tiresome collection of these data.

# OPERATIVE PROCEDURES FOR THE TREATMENT OF STERILITY AND OVARIAN DYSFUNCTIONS*

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THE gynecologist who is primarily a clinician is constantly confronted with problems bearing on ovarian dysfunctions. Some of these problems are satisfactorily answered by the judicious use of gonadotropes and estrogens. Many patients are seen whose complaints refer to faulty menstruation or complete amenorrhea. They give a history, oft repeated, of having been treated by one or many physicians with hormone therapy, sometimes of questionable value and without results. A woman who menstruates seldom, if at all, is greatly concerned as to her future happiness, first as a wife and secondarily as a mother. She becomes alarmed over her supposed lack of femininity and is besieged by many fears, some of them justified, of the future in store for her.

It is a well-known fact that many women have polycystic ovaries and, as a result of that condition, they may have menorrhagia or almost complete amenorrhea. Fundamentally, the disease is due to functional disturbance, the result of imbalance between the endocrine glands.

In 1937, we described six cases in a paper entitled "The Surgical Treatment of Ovarian Dysfunctions," in which it was emphasized that, inasmuch as many patients do not respond in any way to endocrine therapy, a surgical approach was considered justifiable in some instances. The cases presented consisted principally of those treated by excision of a portion of the cortex of one or both ovaries, with very favorable results. In most of the pathological specimens, it was found that there was thickening of the tunica albuginea, increased fibrosis of the ovarian cortex and follicles in all stages of development and atresia. Hypothetically, it was thought that the thickening of the ovarian cortex due to long-continued endocrine dysfunction made it impossible for the follicles to rupture and, consequently, there was a mechanical impediment which we were able to overcome by decortization. Since that time, we have operated upon eleven other similar cases and will present the results.

The operation consists of one of two procedures. In those instances where the ovary is large, but not a neoplasm, a wedge of substance is taken in its longitudinal axis, the defect being closed with interrupted or figure-of-eight sutures of No. 00 plain catgut.

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In most of the cases which we are about to present, however, the process consisted merely of denuding a portion of the cortex, and controlling small bleeding points with mattress sutures of No. 00 plain catgut. Recently, we have used Gelfoam on the cut surface with satisfactory results.

CASE 1.—S. V., aged 25 years, married 3 years, gravida 0, was first seen on April 17, 1937, complaining of sterility associated with menstruation every 6 to 8 months, free, with clots and much pain. Previous estrogenic treatment was unsuccessful. Rubin's test showed patency of tubes, and pelvic examination showed the uterus to be moderate in size and in good position. Both ovaries were large, firm, and very tender, especially the left. May 8, 1937, curettage, insertion of stem pessary, resection of a part of the cortices of both ovaries and appendectomy were done. She menstruated regularly, at 30-day intervals, after the operation and removal of stem, until April 14, 1939, when she was found to be pregnant. She was delivered of a living baby in January, 1940.

*Pathological diagnosis:* Simple cysts of ovary.

CASE 2.—H. B., aged 22 years, single, gravida 0, was first seen on Jan. 14, 1937, complaining of amenorrhea. Last menstrual period, July, 1935. Examination showed both ovaries large, low, and tender. Jan. 18, 1937, curettage and stem pessary insertion, without results. She menstruated once, after estrogenic stimulation, June 6, 1937. Stem removed in September, but no menstruation followed until after operation, on Oct. 27, 1937, consisting of excision of two-thirds of the cortex of each ovary, with incidental curettage and appendectomy. Both ovaries were polycystic, but not sclerotic. Menses continued to be irregular at 2- to 3-month intervals.

*Pathological diagnosis:* Polycystic ovaries.

CASE 3.—D. H., aged 28 years, gravida 0, was examined on Sept. 22, 1942. She complained of a bearing down sensation when on her feet, and of having menstruated only three times in her nine years of married life. Examination showed a small uterus, displaced to the right by a cystic left ovary, estimated to be 8 cm. in diameter. Oct. 8, 1942, operation was performed, consisting of curettage, left salpingo-oophorectomy, resection of cortex of the right ovary, and appendectomy. She has menstruated regularly every 26 to 28 days since that time, but never became pregnant.

*Pathological diagnosis:* Theca cell tumor, left ovary. Follicular cysts, right ovary.

CASE 4.—C. D., aged 35 years, married, para i, was first seen on Feb. 7, 1944. She had menstruated but once, in August, 1942, since the delivery of her first baby, in 1941. Examination showed her to be healthy, but overweight (180 pounds). Pelvic examination showed a relaxed vaginal outlet and ovaries which seemed sclerotic. She was operated upon April 4, 1944. Curettage produced no material. Perineorrhaphy was done. At laparotomy the ovaries were found to be small and sclerotic. The cortices were excised. She menstruated slightly after the operation, but only once (April 25, 1944). This lasted 5 days, but she has never menstruated since. This is thought to have been a case of Chiari's syndrome.

*Pathological diagnosis:* None.

CASE 5.—N. L., aged 20 years, single, was examined on Aug. 28, 1944. She complained of menstruating every two weeks, for a year. She was found to have a left ovarian tumor, 6 cm., which was solid and thought to be a dermoid cyst. She was operated upon Sept. 25, 1944, and found to have a thecoma of the left ovary. Curettage was performed and the left ovary removed. The cortex of the right was partially removed and incidental appendectomy performed. After this procedure menstruation occurred every 30 days. She married and was last seen in June, 1945, at which time she was found to be pregnant.

*Pathological diagnosis:* Thecoma of left ovary. Right ovary, normal.

CASE 6.—M. L., aged 26 years, married 4 years, para 0, was first seen on April 29, 1946. Complaint was that of no menstruation since 1942. Prior to that time, she had been regular, every 28 days. Basal metabolic rate recently, –29%, taking thyroid regularly. Pelvic examination showed the uterus to be small and anterior; left ovary seemed large, probably polycystic. She was given courses of gonadotropes and estrogens, without results. On June 11, 1946, curettage, stem No. 2, left cortectomy and partial wedge excision of the right ovary were performed. She menstruated in August, 1946, and not again until April 26, 1948. With cyclic therapy she has menstruated regularly since that time.

*Pathological diagnosis:* Multiple small simple cysts of ovaries.

CASE 7.—R. G., aged 33 years, gravida i, had had one early spontaneous abortion, in 1942. She complained of sterility. She normally menstruated every 4 to 6 weeks, until May, 1945. She had complete amenorrhea, in spite of hormonal stimulation after this time. Examination showed the presence of a large left ovary. On Feb. 6, 1946, curettage was performed and a segment of the left ovary was removed; right ovary was partially decorticized and both were suspended. On March 8, 1946, she had a free menstruation and has continued to menstruate every 28 days since then, but has never become pregnant.

*Pathological diagnosis:* Simple and corpus luteum cysts of ovary. Atypical cystic hyperplasia of endometrium, slight.

CASE 8.—V. W., aged 30 years, married 5 years, a physician, from another city, consulted me concerning amenorrhea and sterility, on May 6, 1946. Her last menstruation had occurred in July, 1945. Pelvic examination showed that both ovaries were large and sclerotic. Naturally, the tubes were checked and found patent, and the husband was proved to be fertile. On June 26, curettage and stem pessary were followed by resection of a segment of the right ovary, one-third of the cortex of the left, and both were suspended. Three months later, the stem was removed. She menstruated regularly, until Nov. 3, 1946, and on Jan. 13, 1947, she was found to be two months pregnant, and was referred back to her local obstetrician.

*Pathological diagnosis:* Multiple small follicular and luteinized follicular cysts of both ovaries.

CASE 9.—B. J. N., aged 22 years, married 1 year, wife of a physician, was first seen on Dec. 7, 1942. Menstruations were regular until 1941; now occur every 3 or 4 months. Complaint of constant pain in right lower abdomen. Examination showed the presence of large ovaries, both prolapsed, especially the right. On Dec. 9, 1942, the cortex was excised from the right ovary and a segment of the left was removed. Both ovaries were suspended and incidental appendectomy performed. She menstruated regularly every 35 days until June 14, 1944, and on August 24, 1944, she was two months pregnant. She delivered a full-term baby, in March, 1945.

*Pathological diagnosis:* Hyperplasia of tunica albuginea. Multiple follicular cysts. *Comment:* No corpus luteum.

CASE 10.—M. W., aged 27 years, single, was seen on Jan. 7, 1946, complaining of amenorrhea, although she had had some cramps each month, for ten years. Much treatment without results. Examination showed female development and hirsutes, but poorly developed breasts. The uterus was infantile, the ovaries not palpable. On Feb. 12, 1946, curettage was performed and a small stem inserted in the uterus. At laparotomy, both ovaries were found to be very tiny. However, we excised some cortex from the left one and punctured some small cysts in the right. She was given large doses of stilbestrol and a course of Squibb's gonadotropic hormone, alternating. She menstruated for 6 days, starting March 28, 1946, and has menstruated every 28 days since then.

*Pathological diagnosis:* Simple follicle cyst of ovary.

CASE 11.—B. L., aged 25 years, married 5 years, gravida 0, was first seen on Sept. 13, 1947, complaining of amenorrhea and sterility. Last menstruation had been in May, 1946. Family physician had administered estrogens in large quantities. Examination showed the presence of large prolapsed ovaries which seemed thickened and not tender. Operation, Oct. 8, 1947, consisted of curettage, insertion of stem pessary, resection half of each large ovary, suspension of both and incidental appendectomy. Curettage at this time showed the absence of endometrium. Menstruation started on Oct. 30, 1947, and she was regular until May 5, 1948. The last examination was in July, and she was found to be pregnant.

*Pathological diagnosis:* None.

A brief summary of these cases shows that two had theca cell tumors, which were removed. A portion of the cortex of the remaining ovary was resected and both menstruated regularly after the operations. One had menstruated every two weeks for a year, before surgery. One, with polycystic ovaries, had a wedge resection of each and menstruated occasionally. All the others complained of menstruating at rare intervals or not at all. One complete failure was in a 35-year-old patient, who had bilateral decortization and has had symptoms of the menopause since then. This was thought to be an atypical instance of Chiari's syndrome, inasmuch as her amenorrhea followed the birth of a baby with resulting hyperinvolution of the uterus and a long-continued lactation. The remainder, eight in number, had simple cortectomy performed and have menstruated fairly regularly since operation. One unmarried patient, aged 27 years, who had never menstruated in her life, now does so regularly. Five of the cases have become pregnant.

In the past eleven years, we have operated upon twenty cases in which there was pathology complicating sterility, where a major operative procedure seemed justified. The results have been most gratifying, as the following tables will show:

TABLE I. CHOCOLATE CYSTS AND STERILITY. (TUBES ALL PATENT)

| | | AGE | DIAGNOSIS | OPERATION | RESULTS (NO. OF DELIVERIES) |
|---|---|---|---|---|---|
| 1. | Mrs. P.<br>1943 | 34 | Choc. cysts<br>Sterility | Oophorectomy<br>Salpingopexy | 2 |
| 2. | Mrs. D.<br>1943 | 28 | Choc. cyst<br>Sterility | Excision cysts<br>Suspension of ovaries | None |
| 3. | Mrs. C<br>1943 | 30 | Choc. cyst<br>Sterility | Oophorectomy<br>Salpingopexy | 2 |
| 4. | Mrs. M.<br>1946 | 36 | Choc. cyst<br>Sterility | Oophorectomy<br>Salpingopexy | 1 |
| 5. | Mrs. M.<br>1942 | 26 | Choc. cysts<br>Retroversion<br>Sterility | Dilatation and curettage<br>Suspension<br>Resection ovarian cyst<br>Dilatation and curettage | 1 |
| 6. | Mrs. A.<br>1945 | 30 | Fibroid uterus<br>Choc. cyst<br>Sterility | Myomectomy<br>Oophorectomy<br>Salpingopexy | 1 |
| 7. | Mrs. K.<br>1946 | 33 | Choc. cyst<br>Retroversion<br>Endometriosis<br>Sterility | Freeing of cul-de-sac<br>Gilliam suspension<br>Left oophorectomy<br>Salpingopexy | 3 |
| 8. | Mrs. A.<br>1944 | 27 | Cystic ovaries<br>Prolapsed | Resection ovarian cyst<br>Suspension both ovaries | 2 |

TABLE II. FIBROIDS AND STERILITY (TUBES ALL PATENT)

| | | AGE | DIAGNOSIS | OPERATION | RESULTS (NO. OF DELIVERIES) |
|---|---|---|---|---|---|
| 9. | Mrs. K. 1941 | 28 | Fibroid uterus<br>Sterility | Myomectomy<br>Resection of ovarian cyst | 2 |
| 10. | Mrs. D. 1945 | 34 | Submucous fibroid<br>Sterility | Excision myoma, vaginally | 1 |
| 11. | Mrs. A. 1946 | 30 | Fibroid uterus<br>Sterility | Dilatation and curettage<br>Myomectomy<br>Gilliam suspension | 1 |

TABLE III. OLD INFLAMMATORY DISEASE AND STERILITY (TUBES CLOSED OR ABSENT)

| | | AGE | DIAGNOSIS | OPERATION | RESULTS |
|---|---|---|---|---|---|
| 12. | Mrs. M. 1942 | 42 | Right hydrosalpinx (Left tube out) | Salpingostomy | None |
| 13. | Mrs. K. 1937 | 37 | Bilateral hydrosalpinges<br>Sterility | Salpingostomy | None |
| 14. | Mrs. R. 1945 | 28 | Previous bilateral salpingectomy<br>Sterility | Canalization, left cornu | None |
| 15. | Mrs. C. 1940 | 32 | Previous bilateral salpingectomy<br>Sterility | Estes operation | None |

TABLE IV. MISCELLANEOUS

| | | AGE | DIAGNOSIS | OPERATION | RESULTS (NO. OF DELIVERIES) |
|---|---|---|---|---|---|
| 16. | Mrs. D. 1944 | 34 | Retroversion<br>1-child sterility | Dilatation and curettage<br>Gilliam suspension | 1 |
| 17. | Mrs. P. 1943 | 27 | Endometrioma<br>Retroversion<br>3 miscarriages | Dilatation and curettage<br>Excision endometrioma in cul-de-sac<br>Gilliam suspension | 2 |
| 18. | Mrs. S. 1947 | 31 | Chronic pelvic inflammatory disease<br>Left tubovarian cyst<br>Sterility | Left salpingo-oophorectomy<br>Suspension rght ovary | 1 |
| 19. | Mrs. O. 1947 | 31 | Retroversion<br>Sterility | Dilatation and curettage<br>Bilateral salpingopexy<br>Suspension ovaries<br>Uterine suspension | None |
| 20. | Mrs. H. 1941 | 33 | Retroversion<br>Sterility<br>Partial tubal obstruction treated 6 years | Dilatation and curettage<br>Gilliam suspension | 2 |

## Summary

We have presented ten cases in which the patient menstruated seldom if at all, and another who menstruated every two weeks for a year. This was one of those with a theca cell tumor. With one exception the remainder

were benefited by partial excision of the ovarian cortex, also by using a wedge resection in those instances where the ovaries were unusually large. Suspension of the ovaries has been freely used. Five of these patients have become pregnant.

We have also presented twenty cases where major operative intervention seemed justified for the correction of sterility. Eight of these had cystic ovaries, in which the ovary involved was removed and the tube salvaged and suspended so as to increase the chances of an ovum being received in the fimbriated extremity.

Three had myomectomy performed, with good results; four had various operations for closed or absent tubes, all without results. The remaining five were treated by uterine suspension. Of the twenty cases, fourteen have now become pregnant and, to date, have delivered twenty-two full-term living babies.

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## Discussion

DR. FRANK E. WHITACRE, Memphis, Tenn.—Dr. Reycraft's report on the surgical treatment of ovarian dysfunctions introduces a debatable subject. The reported cases are a collection of several procedures. It is commonly accepted that myomectomy in some instances may prove to be good treatment for sterility and occasionally for menstrual disorders, and the essayist's success with this group demonstrates careful selection of cases. It is also commonly accepted that salpingostomy in the presence of chronic pelvic inflammatory disease is not often successful in the treatment of sterility, and this also is borne out by his results.

I am particularly interested in Dr. Reycraft's series of removal of the cortex of one or both ovaries. An explanation of the successful cases might be more than removal of the thickened cortex. The origin of primordial follicles is still an unsettled question. There is some evidence from animal experimentation that follicles may have their origin in the hilum or at its juncture with the mesovarium. It is possible that resection of the cortex of the ovary with the hilum remaining intact may be followed by some degree of regeneration of the ovarian cortex. It is important to study the time interval elapsing between the operation on these patients and the establishment of a more nearly normal menstrual cycle and/or pregnancy, and also whether or not a future laparotomy on the same patient might demonstrate regeneration of ovarian cortex.

My experience with this procedure has been limited, and opinions of my colleagues who have carried out this or similar operations vary from lack of enthusiasm to recommendation. Success in the use of similar procedures has been reported by Stein and also by Jacobson. The degree of success reported by the essayist and other authors presupposes careful study and selection of patients and delicate handling of tissue. In congratulating Dr. Reycraft on his results, it must be understood that this meticulous study is mandatory for success and that wide adoption of this and like procedures would lead to a wave of unnecessary surgery on young women over and above what we already have.

In discussing this problem ten years ago, Douglas brought up the question of postoperative adhesions, to which the essayist agreed that it is of real danger. Hartman has shown that adhesions may, and sometimes do, result from simple ovulation in the primate. With this in mind, what could one expect after surgical denudation of the ovary? Perhaps the use of absorbable sponge material would lessen these dangers.

We all see young women who have had one or more pelvic operations directed at the ovaries where improvement is temporary and the end result unsatisfactory. It is, therefore, a question of careful judgment. Operations on the ovary in young women should be controlled by the specialist. In recent years agencies authorized to establish the standards of hospitals have compelled the consultation of a qualified specialist before cesarean section is permitted to be done, and this has resulted in general improvement. This principle could be extended with benefit to include the subject under discussion.

DR. EMIL NOVAK, Baltimore, Md.—While I have not personally employed ovarian resection for the treatment of amenorrhea per se, I have been interested in the reports of others. It must be remembered that ovarian dysfunction is not a mere plus or minus affair, as would seem to be the case with the thyroid. Furthermore, ovarian dysfunction is most often only an ovarian reflection of disordered function of the anterior pituitary. There are many cases of amenorrhea in which there is an excess of estrogen, many in which there is a deficiency, so that such a procedure as ovarian resection would be a highly random affair unless it were very sharply circumscribed by methods of study still highly unreliable. Many years ago Henkel advised resection of the ovaries for functional bleeding, probably on the basis of an assumed analogy with hyperthyroidism. The results of this plan, long since abandoned, were disappointing, although its revival has been suggested from time to time since then.

I believe it quite probable that ovarian resection might be of value in a small proportion of cases, perhaps of the group in which Stein advocates performance. Any benefit in such cases, however, would seem explainable on the basis of pituitary mediation. As far back as 1928, Lipschütz enunciated the "law of follicle constancy," and I believe that this is probably true. According to this, resection of the ovaries would be followed by the concentration of a continuing pituitary gonadotrophic function upon a reduced ovarian surface, with increased follicle maturation and increased estrogen production as a result. This, to my mind, would explain the good results in a small group better than the mechanism suggested by Stein himself.

The case reports of Dr. Reycraft do not impress me as good evidence for the wisdom of the procedure. In two of his cases, for example, a thecoma of the ovary was removed, and this tumor not infrequently causes amenorrhea. Another patient presented what appeared to be a Chiari syndrome, and in most cases a curettage was done. This procedure in itself may at times be helpful through the still poorly understood coordination between the uterus and the ovaries.

My chief apprehension concerning such a paper is the fact that it might lead to the widespread abuse of ovarian resection for amenorrhea per se. The old dictum of "Either take out the ovary or leave it alone" cannot be accepted without qualification, but in the main the principle is a good one. While resection is easy, it may do far more harm than good, as secondary operations will often show adhesions and possibly angulation of the intestines, angulation of the tubes, and other unpleasant sequelae. Furthermore, in most cases of amenorrhea, it is quite certain that no benefit would accrue from the operation.

DR. GEORGE W. KOSMAK, New York, N. Y.—Doctor Reycraft stated that the stem pessary is employed. I would like to ask him what the indication was for this procedure. I thought it was pretty well abandoned.

DR. REYCRAFT (Closing).—This discussion was really less critical than I expected. It is granted that this is a procedure that should not be done by everybody, as it is very likely to be abused, and I therefore emphasized the fact that I had done it in only 11 cases in 11

years, and I felt I had screened the cases very carefully. Dr. Novak has called attention to the fact that one was a Chiari's syndrome and two had theca cell tumors. We have, doubtless, produced changes in the physiology of the ovarian function, although of course the action of the pituitary gland cannot be ignored.

As far as Dr. Kosmak's question about the stem pessary is concerned, we are disciples of Dr. Weir, who has used the stem pessary many, many years, and in clean cases we feel it has a stimulating effect on the endometrium, and when you are "throwing the book" at cases of this kind you want to do everything you can, and in some instances the use of a stimulating instrument, such as a stem pessary, was perhaps of some benefit.

# A STUDY AND CLASSIFICATION OF PELVIC INFLAMMATORY DISEASE*

ROY W. MOHLER, M.D., SC.D., PHILADELPHIA, PA.

THIS presentation is being made because of my interest in pelvic inflammatory disease and because much that has been written and is being taught about it does not correspond to accepted concepts of the behavior of inflammatory processes in other body structures. Because of these two premises, I believe it might be worth while to present some thoughts which seem to me pertinent. I hope this presentation will promote some discussion and increase our interest in this important subject.

## Definition

Pelvic inflammatory disease can be described as a tissue reaction to some irritant which involves the internal female genitals and their contiguous structures. This reaction causes certain signs and symptoms which may be recognized clinically. The structures involved would ordinarily include the uterus and its adnexa, the parametria in its broadest sense, and the pelvic peritoneum, and sometimes the rectum, sigmoid, and cecum. This definition is basic and corresponds to the accepted concepts of inflammation and its cause in all body structures.

To understand clearly why pelvic inflammatory disease behaves as it does, we must appreciate the two characteristics of the female genital tract which are anatomical and physiological. The anatomical characteristic is the fact that the female genital tract during the procreative period of the individual is patulous and there is normally a communication between the external environment of the individual and the peritoneal cavity, and its fundamental physiological characteristic is its adaptability to procreation. If we consider pelvic inflammatory disease with these fundamental facts as basic, it could be much easier taught to students, and it seems to me that our concepts correlate much better with generally accepted ideas of inflammation in other body structures.

## Symptoms and Signs

The main symptom of pelvic inflammatory disease is generalized pain of varying intensity limited to the lower abdomen. The signs of the condition are temperature elevation of various degrees, rigidity, tenderness and muscle guarding of the lower abdomen, and pain and tenderness of the internal genitals when an effort is made to outline them through the vagina. The blood count shows various changes which demonstrate its reaction to inflammation. The erythrocytic sedimentation time is reduced. Symptoms and signs indicate that the internal genitals and a localized area of the pelvic peritoneum and its contiguous structures are reacting to some irritant by an inflammatory process.

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## Nomenclature

Pelvic inflammatory disease is a dynamic process and the terms acute, chronic, subsiding, spreading, recurrent, and quiescent are all descriptive of some phase of the process which usually can be recognized clinically. The term chronic is not descriptive of the process which follows acute attacks of pelvic inflammatory disease and should be used only when it refers to reactions such as those caused by tuberculosis, foreign bodies, and other agents which induce slowly progressing processes.

## Causes of Pelvic Inflammatory Disease

The irritants which cause pelvic inflammatory disease are many, but may be classified I think into two groups, namely, those of *bacterial origin* and those caused by some physical force or change in the status of the structures in the pelvis.

The inflammatory processes of bacterial origin are thought to be caused most often by the gonococcus, the streptococcus, the staphylococcus, the colon bacillus, the welchii bacillus, pneumococcus, tubercle bacillus, and the mycoses, which are recognized causes. There undoubtedly are others which have been unrecognized. The physical changes in the pelvic viscera which may cause pelvic inflammation are almost unlimited, and I shall enumerate some of the usual ones, viz., ruptured Graafian follicle, endometriosis, twisted ovarian cysts, twisted pedunculated pelvic tumors, degenerating myomas, tubal abortions and ruptured ectopic pregnancies, hemorrhage into pelvic tumors, torsions of the pelvic viscera (uterus, tubes, and ovaries with the torsion of the uterus with the cervix as the axis), ruptured endometrial cysts, diverticulosis of the sigmoid and many others. All of the above conditions have been observed by me, and it is my impression that the reaction induced by these changes is an inflammatory one, and one is justified in classifying all of them as pelvic inflammatory disease with the cause stated as it can be determined. In many instances, the cause cannot be determined definitely and sometimes not at all because the patient has recovered spontaneously from the process which has made further study or observation unnecessary or prohibitive.

The three most common types of pelvic inflammation of infectious or bacterial origin are stated as the gonorrheal, the septic, and the tuberculous. These three types of infectious or bacterial pelvic inflammation have been recognized clinically for a long time.

Pelvic inflammatory processes of infectious or bacterial origin generally can be considered to have characteristic methods of behavior and I think they arise from a focus that communicates with or is contiguous to the internal genitals.

Pelvic inflammatory disease of infectious or bacterial origin seems to extend either by surface extension or interstitial extension.

### 1. Pelvic Inflammation by Surface Extension

It would seem that this type of pelvic inflammation has its origin from a focus of infection in the lower genital tract, that is, an endocervicitis, a urethritis, or a Bartholinitis. I think it is usually transmitted to the upper genital tract by some physical force which mobilizes the organisms from the lower to the upper genital tract. The type of physical force may be coitus, traumatic treatment, high-pressure douches, and activities which would *increase* intravaginal pressure. As the organisms migrate from their original

focus, they extend along the mucosal surfaces of the various pelvic structures and then various local surfaces become involved in an inflammatory process and consequently an endometritis, endosalpingitis, and finally a pelvic peritonitis develops. Perioophoritis and a perisalpingitis usually follow the peritonitis. These processes are rather definite and understandable but since most of our conclusions must be based on observations made when operation was the treatment for them, these statements may seem arbitrary.

These processes appear to run a fairly definite cycle. There is severe pain in the lower abdomen, muscle rigidity, a high temperature reaction, a leucocytosis, and rather definite pelvic findings when the patient is examined vaginally. The clinical reaction to this process lasts about 72 hours, the temperature then subsides, and the physical condition of the patient improves. So far as we can tell clinically and in the few instances where observations have been made at surgical operation, the patient recovers completely, and it would seem that recovery has occurred spontaneously in spite of the fact that the sulfonamides, penicillin, and other antibiotics have been used in the last few years. The reaction of these patients would indicate that the inflammation of the internal pelvis has been a self-limited process, and that spontaneous and almost complete resolution of the process has occurred.

Why do these attacks of pelvic inflammatory disease tend to recur? It would seem that a reinfection develops because of a latent infection in the lower genital tract and it can be assumed that with each reinfection some slight residuum or change occurs in the pelvic structure, and with a number of reinfections, large pelvic abscesses and extensive adhesions, cystic changes in the ovaries, pyosalpinges, and adherent oviducts develop. These extensive changes are most often seen among Negro patients and are less frequently observed with white patients.

This characteristic reaction has been attributed to the gonococcus and until we began using cultures for the identification of the gonococcus, we were satisfied with our conclusions but in the light of present studies for the identification of the cause for these infections, it is my impression that the problem is not so simple and that we shall find other organisms than the gonococcus sometimes responsible for these surface-spreading infections.

### 2. Pelvic Inflammation by Interstitial Extension

This type of pelvic inflammation is most frequently caused by the pyogenic organisms and should be referred to as being of septic origin. The organisms are most frequently the streptococcus and the staphylococcus but other organisms may be responsible. These inflammations result from an inoculation of the organism into a break in the continuity of the protective surface of the genital tract and may, therefore, follow any trauma which has disrupted the genital surface, namely, diagnostic procedures such as dilatation of the cervix and curettage of the uterus, cauterization of the cervix, induced abortion, spontaneous interruption of pregnancy and certain other traumatic phenomena. Septic infections, however, are most frequently associated with the interruption of pregnancy, and, therefore, are often referred to as puerperal infections. These infections are interstitial in their progress and pass by way of the lymphatics and the cellular tissue of the pelvis. The involvement of the pelvic structures per se is secondary to the interstitial process.

These interstitial processes are frequently self-limited and the involvement is very slight. Abscess formation, however, sometimes develops. In a few instances, the process extends either into the blood stream or the peritoneal cavity and a septicemia or spreading peritonitis develops. If the pelvic

structures become involved in this process, it is the interstitial or surrounding areas which are affected and not the mucosal surfaces.

Tuberculous pelvic inflammation is relatively infrequent and can be referred to as a chronic inflammatory process. It can be thought of as developing from a focus of tuberculosis elsewhere in the body and is probably of metastatic origin. From a pathological standpoint it may be a surface process or an interstitial one and its powers for destruction are very extensive.

### Pelvic Inflammation Caused by Changes in the Status of the Genitals

Pelvic inflammatory disease caused by physiological changes in the internal genitals and pre-existing tumors of these structures is a very definite entity and because the patient recovers spontaneously from the process, it is often assumed that a pelvic inflammatory disease of infectious origin has been present. It is my thought that many of these processes are definitely inflammatory processes of noninfectious origin and are serious enough to warrant definite recognition and sometimes prompt surgical treatment.

I shall cite two clinical examples of what I have in mind with the histories of two patients admitted recently to Jefferson Hospital in Philadelphia:

CASE 1.—Mrs. M. W. (6216), aged 36 years, Negro, gravida iv, para iv, was admitted to the Gynecological Ward of the Jefferson Hospital on Oct. 14, 1947, with a complaint of irregular menstrual periods and feeling of fullness in the pelvis. After the birth of her last child in 1937 her periods recurred only once a year. In 1944 she had an attack of "peritonitis" requiring hospitalization elsewhere. When first seen at Jefferson Hospital Outpatient Department on Oct. 9, 1946, a tentative diagnosis of pelvic inflammatory disease and myoma uteri was made. On admission to the Jefferson Hospital Ward on Oct. 14, 1947, she had vaginal bleeding which had been present for three weeks. Pelvic examination revealed the uterus to be normal in size with a tender mass the size of a baseball attached to the right cornu. A preliminary diagnosis of myoma uteri was made. Following examinations the patient developed an elevation of temperature and leucocytosis. These changes were interpreted as indicating a flare-up of a residual pelvic inflammatory disease. On Oct. 17, 1947, the patient showed signs of internal hemorrhage and was operated upon. The abdominal cavity was filled with blood. A solid right ovarian tumor about 7 cm. in diameter was found to be ruptured and bleeding actively from several areas.

Pathological report showed the ovarian tumor to be a granulosa cell tumor.

Our clinical diagnosis before operation and our clinical findings on this patient were those of pelvic inflammatory disease. Observations and studies before operation and the changes in the pelvis at operation indicated a pelvic inflammatory process and it would seem that the accident which occurred to this pre-existing tumor was definitely responsible for the inflammatory process.

CASE 2.—Mrs. B. O., aged 44 years, was admitted to Jefferson Hospital on Jan. 17, 1947, with a chief complaint of abdominal pain of three days' duration. The patient had been well until the third day of her menstrual period, Jan. 14, 1947, when she experienced a continuous pressure-like pain throughout her abdomen. The pain increased in severity the next two days and was associated with an elevation of temperature of 100° F., mild chills, general malaise, and headache. Her family doctor prescribed oral penicillin which was taken for eighteen hours before admission to the hospital. On admission to the hospital the patient had generalized lower abdominal tenderness. On pelvic examination it was found that the uterus was incorporated in or attached to a pelvic mass which filled the pelvis and extended to the level of the umbilicus. The mass was soft but not definitely cystic. The impressions were an ovarian tumor or soft fibromyoma of the uterus. The patient was operated upon on Jan. 25, 1947. A large multilocular, cystadenocarcinoma of the left ovary the size of a five

months' pregnancy was found. The tumor had apparently ruptured previously as there was a small amount of dark watery fluid in the abdomen which may have accounted for the acute symptoms. The tumor was extensively adherent to the rectosigmoid which was pushed into the right side of the pelvis and lower abdomen. Four days after operation the patient was afrebrile. She had an uneventful postoperative course. Here again the pre-existing pelvic tumor underwent some change inducing symptoms and signs of pelvic peritonitis which actually was responsible for recognizing the pressure of the malignant tumor. Actually the patient was admitted to the hospital for what was recognized as a pelvic inflammatory disease and after treatment with operation we determined the cause of the inflammatory process as a pre-exising adenocarcinoma of the ovary.

## Discussion

There are many phases of this important subject which have not been discussed in this presentation. The large areas of loculated exudate, the difference in extent and consistency of adhesions observed at operation, the time and the indications for operation have not been mentioned. The purpose has been to focus the attention of this organization on this important problem and to try to think of it in terms so that medical students and house officers and physicians generally would understand that pelvic inflammatory disease is an entity because of anatomical and physiological characteristics of the female, but the inherent reaction of the individual to the process is not much different in the female pelvis than it is in other body structures. There may be some question about my suggestion that pelvic inflammation of non-infectious origin exists. Many of the accidents which occur in pelvic tumors, ectopic pregnancies, endometriosis will cause immediate reactions which are referred to as the phenomenon of shock, but if this reaction is not observed immediately or if this condition is not severe enough to warrant immediate treatment, an inflammatory reaction develops which is characterized by the stated symptoms and signs of pelvic inflammatory disease and if surgical treatment is instituted this fact will be demonstrated.

## Summary

1. This presentation has been made with the idea of stimulating some interest in a very important gynecological problem.

2. I have tried to correlate it with inflammatory processes observed elsewhere in the body.

3. I have suggested that pelvic inflammatory disease is a reaction of the internal female genitals and their contiguous structures to some irritant.

4. The irritant may be either of bacterial origin or of physical origin.

5. Pelvic inflammatory disease is a term which has a definite connotation and should be used carefully.

6. I have indicated that the inflammatory processes of infectious origin develop by means of surface extension from a focus in the lower genital tract or by means of interstitial extension from a focus somewhere in the genitals or other body structures.

7. I have suggested that not all surface-extending infections are of gonorrheal origin since cultures and smears do not indicate the presence of these organisms.

8. Pelvic inflammation may be caused by changes in the status of pre-existing tumors and structures in the pelvis or physical changes in the structures of the pelvis and not be of infectious origin.

## Discussion

DR. J. MASON HUNDLEY, Baltimore, Md.—At the University of Maryland we strongly emphasize the conservative treatment of tubal disease, especially that due to the gonococcus and with the advent of chemotherapy the incidence of necessary operative procedures has greatly decreased, approximately only 15 per cent of the patients coming to surgery. With us the indications for operation are as follows: 1. painful, fixed retrodisplacement; 2. adhesions with symptoms; 3. metrorrhagia and menorrhagia associated with marked dysmenorrhea; 4. large hydrosalpinges or tubovarian abscesses; 5. repeated attacks of infection.

Conservation of tissue is stressed, especially in the gonococcal group. However, with advanced pathology due to the streptococcus or tubercle bacillus, the procedures are of necessity more radical for here the organisms are long-lived and virulent which is in contrast to the gonococcus.

An interesting historical digression is in regard to the specificity of the gonococcus and is of especial interest to the physicians of Baltimore, for it was here that Phillipe Ricord, between 1830 and 1840, did his monumental work inoculating hundreds of men with gonorrheal pus and in none was he able to produce syphilis. Even at this late date, due to the teachings of Sir John Hunter, it was believed that gonorrhea and syphilis were the same disease in spite of Sir John's developing syphilis after inoculating himself with secretions supposedly from a case of gonorrhea.

The study of tuberculous salpingitis is of interest primarily due to its apparent infrequency. In a survey of 1,092 patients with salpingitis there were only 22 due to the tubercle bacillus, an incidence of 0.2 per cent. The majority of textbooks state the occurrence of tuberculous salpingitis in the order of 5.7 per cent; this decline in incidence is, I am sure, due to the education of the public as to preventive methods and the more intelligent and modern procedures of therapy. Some years ago the second most common cause of death was due to tuberculosis, whereas today this condition occupies the fifth position. There is a definite decrease in the incidence of pulmonary tuberculosis which is the prime etiological factor in tuberculous salpingitis.

Figures from the Department of Health of the State of Maryland definitely support this opinion in regard to the white race but not so significantly in the Negro. In the years 1921 to 1925, the death rates per 100,000 population were 94.3 for whites and 281.4 for Negro. Now compare this to the figures for the five-year period, 1941 to 1945. We find a marked decline in the white race from 94.3 to 39.6 per 100,000 population; the decline in the Negro race is not so striking, namely 281.4 as compared to 184.7 per 100,000 population. The present death rate from tuberculosis in the Negro race is still too high but in spite of this there has been a marked decline in the incidence of tubal tuberculosis. The reason for this is difficult to ascertain.

Another aspect of the paper deals with recurrent attacks of pelvic inflammatory disease. These recrudescent attacks must be due to new infection from the urethra, cervix, or consort, or from increased viability of dormant cells in the wall of the tube. In 1921 Curtis carried out a rather exhaustive study on the viability of the gonococcus in the tubal wall and lumen with the resulting conclusions: "It has almost never been possible to obtain gonococci in culture from thoroughly ground Fallopian tubes removed from patients who have been free from fever and leucocytosis for a period of more than ten days or two weeks. The Fallopian tube appears, therefore, not to be a focus for chronic gonorrheal infection. Persistently active gonorrhea of the tubes is evidently ascribable either to recurrence from without or repeated invasion of bacteria from the chronically infected lower genital tract."

This opinion has prevailed for a number of years. However, in 1938 Studdiford studied this same problem and his findings did not support those of Curtis. His conclusions, based on a study of 24 patients with gonococcal salpingitis, were as follows: "Contrary to previous reports the Fallopian tubes may remain as active foci of gonococcal in-

fections for long periods of time. Many cases regarded as acute exacerbations of chronic salpingitis may be due to recrudescence of residual infection rather than to reinfections.''

With such divergent opinions existing we thought it worth while to restudy the problem. The selection of cases is important for we did not wish to subject young women with acute gonococcal disease to radical surgery when the condition could be alleviated in a large measure by the use of chemotherapy.

Our study is in its beginning and the majority of the patients studied are those with chronic salpingitis frequently associated with uterine fibromas. There is no debate as to the presence of organisms in the acutely inflamed tube but it is in the chronic conditions that there is a difference of opinion.

The technical procedure is as follows: A box with two glass sides is set up with an ultra-violet apparatus placed in the top. After an exposure of thirty minutes the air contained in the box is sterile as proved by cultures.

Smears and cultures from the lumen of the tubes are carried out in this sterilized atmosphere. Cultures are made on chocolate agar and incubated under 10 per cent carbon dioxide at atmospheric pressure. Sections of the tubal wall are macerated in a mortar using sterilized sand and sterile water.

To date one patient with subacute salpingitis and ten patients with chronic tubal disease have been studied bacteriologically. Six of these patients had associated uterine myomas. The patient with the subacute lesion showed positive gonococcal smears and cultures of the cervix and urethra while the tubes showed negative results on smear, cultures from lumen, and also cultures of macerated tube wall. Of the ten patients with chronic salpingitis, four showed no evidence of tubal infection. In the remaining six patients the tubes, cervix, and urethra were positive for gonorrhea on smear and culture and cultures of the macerated tissue. In one of these patients the examination of the cervix and urethra was not done.

It is obvious from this preliminary study that we can come to no definite conclusions as yet. However, it is clear that tubal infection persisted in six of the patients studied who had long-standing chronic disease. This is suggestive that the gonococcus may be present in the tube after acute symptoms have subsided and the condition has become chronic.

DR. WILLARD R. COOKE, Galveston, Texas.—I regret that I have been unable to obtain an adequate concept of Dr. Mohler's philosophy and ideas from a fifteen-minute condensation of so protean a subject. I gather that he includes the phenomena of repair, regeneration, and foreign-body reaction in his definition of inflammation, in addition to the true inflammatory reactions to trauma of mechanical, chemical, bacterial and protozoal origin. In any discussion of inflammation, the general and the peculiar local defense-mechanisms must be taken into account. I can agree that, in the preadolescent child, the phenomena of inflammation are probably identical with similar processes occurring elsewhere in the body. With the onset of adolescence, however, a great number of processes develop which are peculiar to the genital tract and modify greatly the behavior of inflammation. The vaginal epithelium, hitherto extremely vulnerable to noninvasive bacteria (and to trauma) becomes highly resistant. As normal physiologic processes various types of cyclic trauma occur, with inevitably resultant semi-inflammatory reactions, the creation of portals of entry, fluctuations in both general and local defense, etc. In the ovary there occurs the minor trauma of rupture of the follicle and the introduction of foreign bodies in the form of extravasated blood and of the dying and degenerating newly formed corpus luteum. In the uterus there occurs the frequent and considerable trauma of the loss of the endometrium, and the relatively infrequent but tremendous trauma incident to the termination of pregnancy. It is from the physiologically normal repair of these injuries that the controversy between the general and the gynecic pathologists in regard to ''endometritis'' has arisen. In the perineum there is evidently a specific local defense mechanism against the anorectal

and other local pathogenic organisms. We have demonstrated this repeatedly by using the instruments contaminated by episiotomy for the removal of moles located elsewhere, with 100 per cent infection and destructive inflammation of these secondary wounds (the episiotomy wound healing promptly and with only the inevitable minor inflammatory reaction).

Moreover, the behavior of certain infecting organisms in the genital tract as compared with their behavior elsewhere must be remembered. It is necessary to mention only the trichomonads; the differences between the reactions to the gonococcus in the genital tract and in the joints; and the extraordinary behavior of *C. welchii,* which in the genital tract varies from innocuous infestation to extreme toxemia and death—with an extreme rarity of any major gangrenous process.

Finally, in the third phase of gynecic life, the lowering of resistance through atrophy, local anemia, and fibrosis is markedly greater than in any other part of the body.

DR. HARVEY B. MATTHEWS, Brooklyn, N. Y.—Dr. Mohler has reviewed in a very remarkable manner the question of pelvic inflammatory disease as we understand it, but whether we can agree with his bacterial or mechanical idea, as it were, we are not quite sure.

I have always felt and taught that pelvic inflammatory disease was due to infection of bacterial origin. We speak, very properly, of pelvic infections and think that as a result of such infections we have pelvic inflammatory disease. Just as in any inflammation we recognize the acute and chronic stages of the disease, every infection anywhere in the body must pass through these stages. It frequently happens, for the good fortune of the patient, that such infection clears up entirely due to the many factors controlling infectious processes in general, and the pelvis is left free of pathology. On the other hand, there is usually some residual pathology following these pelvic infections. Therefore, I cannot agree wtih the author when he says, ''the term chronic is not descriptive of the process which follows acute attacks and should be used only when it refers to reactions such as those caused by tuberculosis, foreign bodies, and other slowly acting processes.'' Any bacterial or septic infection certainly does become chronic and may or may not leave in its wake some residual pathology.

Now, as to the pelvic inflammatory disease of nonbacterial origin, again I must disagree somewhat with Dr. Mohler. Of course, such acute inflammatory states do occur but they are complications secondary to some pre-existing pelvic lesion or tumor and are due to mechanical causes; e.g., ruptured ectopic ovarian cyst with twisted pedicle or degeneration of a fibroid due to interference of circulation to the tumor. In these conditions a correct differential diagnosis always gives the clue to the proper treatment, operative or conservative.

In conclusion, I believe that pelvic inflammatory disease is a well-recognized clinical-pathological entity caused by bacterial invasion and that what Dr. Mohler terms pelvic inflammation of nonbacterial origin is merely a mechanical complication of a pre-existing pelvic lesion or tumor. Of course, there may occasionally be infection also.

I agree most heartily with Dr. Mohler that pelvic inflammatory disease is a term which has a definite connotation and should be used with care and discretion, much more accurately than it oftentimes is.

DR. E. D. PLASS, Iowa City, Iowa.—More recently, the term ''pleuropneumonia-like organisms'' has occasionally invaded the literature dealing with pelvic infections in women, and, as more bacteriologists become familiar with this curious organism, the use of the term will become more common. This is particularly true since these organisms may develop by a process of pleomorphism from many gram-negative bacilli and cocci under the influence of extraneous factors, such as penicillin. Consequently, interpretation of its etiologic role in patients previously treated with this antibiotic is difficult or impossible.

Pleuropneumonia-like organisms or ''L''-forms are evidently a part of the vaginal flora in many normal women, but thus far have not been implicated in vaginal infection. In our material representing cultures for 312 consecutive gynecologic admissions, there were 81

instances, 26 per cent, in which "L"-forms were cultivated. The figure agrees well with the few others reported in the literature. In addition, my associate, Robert J. Stein, was able to demonstrate the organisms in two cases of pelvic inflammatory disease, including one pelvic abscess, but is unable to interpret the findings with assurance.

The first case was in a thirty-year-old woman with a large acute pelvic abscess which had developed marked symptoms during the preceding week. On admission, Dec. 16, 1947, the temperature was 102.2° F. and soon rose to 104.4° F., the white blood count was 18,750 per mm. with 75 per cent polymorphonuclear leucocytes. Penicillin, 50,000 units, was given intramuscularly soon after admission but had little effect on the temperature. On December 18, posterior colpotomy released 300 c.c. of thick pus; a drainage tube was inserted. The temperature dropped promptly to 100.0° to 101.0° F. where it remained for 5 days, and then fell slowly to normal. She was discharged on Jan. 23, 1948, quite symptom-free, but returned to the outpatient clinic May 29, 1948, complaining of a dragging sensation in the right lower abdomen and slight fever. Both adnexa were thickened and slightly tender, and there was a golfball-size mass in the cul-de-sac. Aspiration of this mass yielded a few c.c. of bloody fluid.

The pus obtained at colpotomy revealed a pure culture of pleuropneumonia-like organisms, while the bloody fluid from the small mass aspirated five months later showed only Bacteroides. It is reasonable to assume that the pleuropneumonia-like organisms obtained in the first culture represented a pleomorphic variant of Bacteroides which later reestablished its identity, but it is not clear whether the abscess was due to the pleuropneumonia-like organisms as such, or whether the original infecting agent had been Bacteroides, which had then under the influence of penicillin completed its pleomorphic change in the forty-eight hours before colpotomy. In any event, neither of these organisms is commonly considered in pelvic inflammatory disease, and yet it seems obvious that one or the other must have been the etiologic agent in this case.

The second case, gonorrheal pelvic inflammatoy disease, represents more clearly the pleomorphic change. This 15-year-old girl had the correct diagnosis made by her home physician, who had prescribed some sulfonamide, which was taken for two days before admission on Feb. 16, 1948. There was evidence of acute gonorrheal salpingitis, and positive cultures for *Neisseria gonorrheae* were obtained on Feb. 16, 19, and 25, 1948. Upon establishment of the diagnosis, penicillin was administered intramuscularly in 100,000 unit doses every three hours for eight doses. On February 27, the day after conclusion of the penicillin therapy, a cervical culture revealed no gonococci but many colonies of pleuropneumonia-like organisms.

Pleuropneumonia-like organisms were first found in cattle and are now recognized as the cause of bovine pleuropneumonia. They are generally classified as bacteria, but in their pleomorphic development may produce forms that are filtrable and invisible. In contrast to the viruses, they can be grown on serum-enriched artificial media. The colonies are rarely visible and consequently are overlooked unless a special search is made under the low power of the microscope. The organisms are too fragile to permit study by usual methods and must be examined in the stained surface layers of solid media.

There is some confusion in the diagnosis due to the fact that pleomorphic forms of certain common gram-negative bacteria resemble the pleuropneumonia-like organisms so closely as to defy differentiation. This type of pleomorphism is evidently more common when other bacteria are subjected to the influence of penicillin. Consequently, it is impossible to determine the clinical significance of "L"-forms in patients who have been treated with this antibiotic.

In males, there is no reasonable doubt that pleuropneumonia-like organisms produce urethritis and prostatitis, but the place of the "L" forms in the etiology of pelvic inflammatory lesions in women is not so clear. Various authors have reported its occurrence in vagina flora of from 6 to 26 per cent of normal women, and in up to 75 per cent of those with pelvic inflammatory conditions. Dienes and his group report cultivation of the organism from six Bartholin abscesses and from two pelvic abscesses.

The cases are presented as a part of this discussion to emphasize the need for more work on the etiologic relation of the "L"-forms to pelvic inflammatory disease in women. Since the organisms are resistant to penicillin, it is conceivable that they may be the causative agent in many penicillin-resistant infections in the female generative tract. It should furthermore be emphasized that the indiscriminate employment of penicillin may be producing pleomorphic variants of common bacteria, which have pathogenic properties and which cannot be controlled by penicillin.

DR. MOHLER (Closing).—I admit that I made an attempt to cover a rather large problem in a relatively short period of time. I tried to emphasize in my presentation that pelvic inflammatory disease needs reconsideration. I think Dr. Hundley brought that out in his discussion when he stated that the dictum that Curtis laid down in 1921 was not refuted until Dr. Studdiford made his presentation a few years ago. Dr. Cooke, I think, brought out a number of important points and I feel very positively that when patients are admitted to the hospital very often with a pelvic inflammation they have every sign and every symptom of pelvic inflammation but there is no evidence of infection which can be determined.

This problem needs to be considered and our whole conception of pelvic inflammatory disease I think needs reconsideration and a good deal of thought.

# RETROPERITONEAL LYMPH NODE DISSECTION IN CANCER OF THE CERVIX*

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THROUGHOUT the world for the past fifteen years the accepted form of therapy for patients afflicted with cancer of the cervix has been the combined use of x-ray and radium. In recent years the results from this form of treatment have become known. Critical evaluation of the results is now under consideration. While the results are considerably better than those obtained from radium alone, the initial enthusiasm, just as in the case of radium which supplanted surgery, has not been maintained. The fact remains that while survival statistics have improved they have apparently reached a plateau, at a level which can hardly leave the therapist with a sense of complacency as to his accomplishments. Despite our best efforts to control the disease through early detection and more effective therapy, too many patients die of the disease. The statistics from the different clinics vary, depending upon the type of material, measured by the extent of the disease that is presented to that clinic. If, for example, an alert medical profession and cancer-minded public produce more cases in the early stages of the disease a higher over-all cure rate may be expected. Nevertheless, approximately 60 per cent of the patients with cancer of the cervix die. Moreover, and here lies the challenge of this form of malignant disease, the majority die with the disease sharply confined to the pelvis. To be sure certain patients, usually with Grade III lesions, will die of remote metastases to lung and bone but by far the greater number will come to a terminal issue with extensive disease in the pelvis alone.

Because of dissatisfaction with the results from the combined use of radium and x-ray, a highly critical eye has been turned on the method of introducing an adequate cancerocidal tumor dose to the primary lesion. The revival of the interest in the colpostat is an indication. The literature begins to produce critical assays of the methods of applying interstitial platinum needles of varying lengths and strengths together with a consideration of the time elements involved. External radiation concerns itself with the increasing use of larger voltage x-ray machines employing new portals, or a more intelligent use of the old portals of entry. The primary consideration of both the radium and x-ray therapeutist is to deliver a more effective cancerocidal dose to the tumor site without producing the destructive side

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effects such as damage to bladder, bowel, and skin. Inasmuch as 80 per cent of the cases of cancer of the cervix have extended beyond the confines of the cervix when first seen, the tumor site to which an adequate tumor dose must be delivered varies widely with increasing chance of visceral damage in the face of effective therapy.

As a result of this experimentation in the more intelligent applications of the improved tools for administering radiation there has recently developed a philosophy of therapy that would appear to be most healthy. Formerly there had been a great tendency to standardize therapy. The patient and her disease were made to fit into a planned form of therapy based on the tools available. It mattered little that an individual patient might not adapt herself to the type of therapy laid down for her sight unseen. With a wider variety of the implements for the application of radiation available, plus a more intelligent conception of what we are trying to accomplish, there has developed a tendency to individualize in the treatment of the patient.

Further individualization may appear when the role of surgery finds its proper place in the armamentarium of therapy. It is true that radiation will cure most but not all cancer when delivered in proper dosage at a proper site. There remains the radiation-resistant case well known to us all. Much work is now being done based on the use of the vaginal smear and cervical biopsy of both tumor and normal tissue to determine if possible which cases will prove to be radiation resistant. If such a yardstick is to be made available surgery may find a place in the treatment of cancer of the cervix for other than the early case in a favorable operative risk. It would be unintelligent indeed to subject a patient to a form of therapy destined to failure from the start.

In addition to the problem of the radiation-resistant case there arises a highly controversial question as to the effectiveness of x-ray therapy in dealing with extension of the disease to the regional nodes found in the obturator, hypogastric, and iliac areas. An increasing amount of evidence accumulates to bring the efficacy of x-ray therapy for other than local disease under a serious cloud of doubt. This same question has been raised in other more exposed areas than the deep-seated nodes of the pelvis. Little enthusiasm is held for x-ray therapy directed toward nodes involved with disease in the neck or axilla from primary lesions in lip, tongue, or breast. Moreover, these areas are not only superficial but confined. It is perhaps unreasonable to expect that radiation could be expected to deliver a cancerocidal dose to the tumor without injury to other vital structures such as bowel when the potential area of involvement covers such a wide area, at varying depths from the skin.

To what extent the regional nodes are involved in cancer of the cervix is not accurately known. We know that patients die of their disease without distant metastases. Certainly there is no satisfactory clinical appraisal for such evaluations are notoriously inaccurate even in such areas as groin, neck, and axillae where a 30 per cent error is found. Clinical estimates are no more

accurate in the pelvis. Our staging of the extent of the disease is at best a rough appraisal. Confirmation of this can be found in the series of one hundred radical operations performed by Dr. Meigs in a group carefully selected as having early lesions. Seventeen per cent of positive nodes were found in this selected group of Stage I cases, while 28 per cent were found in early Stage II patients. Taussig in a large series employing his intra-abdominal pelvic lymphadenectomy found 25 per cent of the nodes involved in disease in these areas. In the advanced stage of the disease 66 per cent were found to have positive nodes in a recent operative series of 20 patients subjected to pelvic exenteration. The regional nodes do become involved in disease in an appreciable number of cases.

Based on the assumption that x-ray treatment will not adequately care for the regional metastases in the iliac, hypogastric, and obturator areas, a surgical approach to this problem, which is still in an experimental stage, was suggested by one of us (Nathanson). Without detracting from the established form of treatment by x-ray and radium a surgical attack on the distant nodes is added after there is a reasonable assurance that the local disease has been cured. To date no attempt has been made to alter the established plan of radiation therapy. The portals of entry continue to include the nodal areas without consideration of the fact that these regions will be exposed surgically later.

This same point of view was widely publicized by Taussig who earlier convinced himself that x-ray would not cure diseased nodes and advocated a surgical approach to the pelvic lymph nodes through an abdominal exploration. The philosophy remains the same. The present experimental approach is extraperitoneal.

## The Operation

The operation has been performed in two stages at weekly intervals though there is no major objection to doing a bilateral dissection at the same time particularly in a young, thin patient.

The incision is made as in a herniorrhaphy from the anterior superior spine to the spine of the pubis, the length of the incision depending on the size of the patient. The external oblique fascia is divided in line of fiber and the round ligament identified. This is a most important landmark for medial to its point of emergence from the internal ring the deep epigastric vessels lie on the peritoneum. The gloved finger is inserted in the internal ring and directed laterally with the line of incision through the external oblique muscle being made employing the finger as protection to the underlying peritoneum. A cuff of muscle approximately 1 to 1.5 inches wide should be left on the side of the inguinal ligament to make easier the subsequent anatomical restoration of the wound. The incision is carried through the conjoined tendon to the pubic spine. The round ligament is then divided and turned upward to expose the deep epigastric vessels lying on the peritoneum. The anatomical relationship of the round ligament to these vessels is most helpful in a fat patient where the artery and vein may be obscured by fat. The structures are individually traced as far as possible to their point of origin from the external iliac artery and vein and are separately divided and ligated. This is a most important step and should be done before any attempt is made to strip

back the peritoneum from the inguinal ligament and the underlying muscle. Once this is accomplished the peritoneum strips bloodlessly and with ease, and with the chance of tearing reduced to a minimum. The psoas muscle is exposed at the lateral side of the exposed area while the bladder makes up the medial wall. The external iliac artery with the vein beneath are exposed lying beneath a collection of fatty areola tissue containing the lymphatics and their accompanying nodes. As the peritoneum is stripped upward and medially to expose the common iliac the ureter can be visualized lying on the peritoneum medially. Moist gauze packs are placed to hold back the peritoneum and the bladder. The obliterated hypogastric artery is readily traced as the terminal branch of the hypogastric artery. The ureter lies medial to the artery on the peritoneum. The vaginal, superior vesical, and obturator arteries are readily exposed. The uterine is not visualized for it lies on a deeper plane. No attempt is made to carry the dissection medial to the ureter. It is assumed that the concentration of x-ray therapy is adequate to care for disease in this area. The obturator nerve is not sought at this stage of the dissection but may be exposed lying deep and lateral to the external iliac vein.

The dissection is begun at the inguinal ligament. The medial and lateral circumflex veins course along the bony pelvis just below the inguinal ligament. Troublesome bleeding may follow damage to these veins coloring the tissues and handicapping the rest of the dissection. The origins of the deep epigastric vessels are again identified, ligated, and sectioned. The common trunk of the circumflex veins crosses over the external iliac artery about one-half inch proximal to the origin of the epigastric vessels. This may be spared. An occasional small venous branch may come off the underside of the external iliac vein but otherwise no other important vessels are encountered. The dissection proceeds from the inguinal ligament toward and along the common iliac artery to the bifurcation of the aorta. The artery and vein are stripped clean. The dissection is then carried down along the hypogastric artery, cleaning out the space between the junction of the two vessels. Nodes are often found in this area. Depending upon the extent of radiation response this tissue may or may not be dissected as one block of tissue. It is usually inadvisable to attempt to remove the nodal areas along the external iliac and common iliac areas as a block dissection with those in the obturator area.

This area is attacked separately by first identifying the obturator nerve as the external iliac vein is retracted with the gloved finger in a lateral direction. Considerable difficulty from bleeding may be encountered from a plexus of veins lying deep to the obturator nerve. Inasmuch as no nodes are found in this area the depth of the dissection is marked by the anatomical position of the nerve. The fatty tissue bearing the nodes is then removed from the obturator space and the undersurface of the external iliac space so that the bare bone of the bony pelvis is seen. The wound is then reconstructed as in a herniorrhaphy.

The ease of dissection of the fatty areola tissue from the vessels varies with the extent of radiation reaction in this tissue. At times sharp knife dissection is required. At others the surgery proceeds rapidly and with ease.

There appears to be little relation in the extent of radiation reaction to the size of the dose, the voltage of the x-ray machine, or the duration since x-ray therapy. At times the extent of the reaction may vary on the two sides of the same patient.

## Comment

It is our feeling, based on considerable experience in dissection of these node-bearing areas in the radical hysterectomy for carcinoma of the cervix with dissection of nodes, that better exposure can be obtained than is possible through the abdomen. Because of the extra-abdominal attack the operation has wider applicability than obtained from the intra-abdominal approach. The obese patient who by her very size reduces her chance of effective treatment with radiation is not further denied a chance of cure through surgery because of the technical difficulties of an intra-abdominal exploration. In a group of fifty patients subjected to this procedure the average weight was 160 pounds, including two patients weighing 240 pounds. The mean average was 154 pounds.

The morbidity has been low. Three instances of sepsis were noted occurring in patients weighing 210, 225, and 245 pounds. The final result was satisfactory without the formation of a hernia despite the fact that fascial slough was present in all three. Some apprehension was felt when sepsis occurred in an operative field which opened up the entire retroperitoneal space. These fears were happily not supported. Transient lower leg edema was noted in 10 per cent.

The mortality has been disturbing—4 per cent. There have been two deaths from pulmonary embolus. The operation is staged at weekly intervals. In both instances the fatal embolus came without clinical warning four and ten days after the second stage. The primary source of the embolus was found in the opposite popliteal space in both instances. In one instance positive nodes were encountered; in the other, none. No other deaths were encountered. Much consideration has been given this problem. It has been our desire to keep this operation as simple as possible to remain effective. The division or ligation of the external iliac vein in continuity will not invariably bring edema of the extremity later but is felt to be inadvisable. Ligation of the common iliac can readily be accomplished for the exposure is excellent. It would complicate the surgery to a certain extent. Heparinization might complicate the second stage of the procedure. There is no violent contraindication to performing the operation in one stage. The same disadvantages may be advanced that apply to bilateral hernia repair in an obese patient. Satisfactory solution to this problem must be found to justify the procedure.

The sole consideration in the selection of the suitable case for this operation procedure revolves around the evaluation of the chance of local cure three or more months after completion of the full course of radiation therapy. The estimate is based on clinical appraisal, vaginal smear, and biopsy (Table I).

TABLE I

| | MASS. GENERAL | PALMER | PONDVILLE | AVERAGE |
|---|---|---|---|---|
| Interval radiation to operation | 9.2 months | 4.2 months | 8.7 months | 7.4 months |
| Age | Youngest patient 21 years<br>Oldest patient 72 years | | Mean age 51 years<br>Average age 53 years | |
| Weight | Low weight 113 pounds<br>High weight 245 pounds | | Mean weight 154 pounds<br>Average weight 160 pounds | |

Mistakes have been made in the proper evaluation of the possibilities of local cure for there have been seven cases, or 14 per cent, where the disease has recurred locally following the dissection of the glands. It is interesting

that all occurred in the group that were found to have positive nodes at the time of the dissection. Not all of the instances of positive nodes manifested local disease at a later date but 50 per cent did.

The uncertainty as to whether local disease has been controlled has kept down the number of gland dissections that have been performed. It may be a better policy to do the dissection after a set period of time, perhaps after a few months, in that group of cases where no obvious disease is present. To perform the operation too soon after completion of radiation is to forego the advantage to be gained by the progressive sclerosing action of x-ray. To do it later, one may miss the opportunity of early attack on the nodes which have become involved in disease.

It will be noted that the tabulations involve statistics from three different hospitals. In these institutions the manner of application of radium which always follows x-ray therapy remains fairly constant. In all the central applicator containing 100 mg. of radium salt is supported by interstitial platinum needles placed around the periphery of the growth. It has been the custom in the past to set the total dose to be given at 4,500 mg. hr. That this method of application is outmoded we are well aware; for the purpose of this study it has the advantages of constancy.

The preliminary x-ray therapy varies widely both as to voltage of the machine and to the actual amount of the dosage given. For example, at the Massachusetts General Hospital a 1,200 kv. machine is in routine use, while at the Palmer Memorial Hospital they employ a 400 kv. and at Pondville Hospital a 200 kv. therapy unit. The recorded doses are measured in air (Tables II and III).

TABLE II

| X-RAY FACTORS | MASS. GENERAL | PALMER MEMORIAL | PONDVILLE |
|---|---|---|---|
| Kv | 1,200 | 400 | 200 |
| Portals (pelvic) | AP—15 pts.<br>AP and Rt. Obliq.—2 pts. | Rt. and Lft. Ant.<br>Rt. and Lft. post.—10 pts. | Intravag. and 4 Pelvic Ports—3 pts.<br>Rt. and Lft. Ant.<br>Rt. and Lft. Post.—19 pts. |
| Portal size | 15 × 15—13 pts.<br>12 × 12— 3 pts.<br>10 × 15— 1 pt. | 10 × 15—10 pts. | 10 × 15—15 pts.<br>10 × 10— 7 pts. |

TABLE III

| X-RAY FACTORS | MASS. GENERAL (1,200 KV.) | PALMER MEMORIAL (400 KV.) | PONDVILLE (200 KV.) |
|---|---|---|---|
| Daily dose in r-units | 300 r.—11 pts.<br>400 r.— 6 pts. | 300 r.—9 pts. | 300 r.—8 pts.<br>200 r.—2 pts. |
| Total dose | 14 patients received between 6,000 and 8,000 r.<br>3 patients received between 3,000 and 5,000 r. | 7,200 r.—9 pts. | 14 patients received between 5,000 and 9,000 r.<br>8 patients received between 12,000 and 20,000 r. |

It is our hope that some information might be forthcoming as regards the relative effect from machines of different voltages as well as dosages. While the groups are roughly comparable in numbers they are obviously too small to be of any statistical significance. This tabulation (Table IV) alone is of consequence though here too the groups are too small to have much

meaning. The over-all finding of 28 per cent of positive nodes following complete radiation is important. Actually this is nearly the same figure that Dr. Meigs found in the Wertheim group combined with bilateral pelvic lymphadenectomy where no radiation had been given. In view of the small numbers involved, it cannot be said that radiation of the involved nodes has been ineffective. It does, however, indicate a trend.

The finding of 12 per cent of positive nodes in the patients treated with the 1,200 kv. machine may be important if the same trend holds for a longer group of cases. Against this trend is the finding of 36 per cent where the 400 kv. machine was used while the same percentage is noted from the 200 kv. instrument. In the latter group there has been a wide variation in the total dosage given.

It would appear that the voltage of the machine employed for therapy may have some bearing on the efficacy of treatment, but one may question whether the size of the dose is as important as the sensitivity to radiation of both tumor and patient.

For example, one of the patients received 21,000 r. measured in air employing a 200 kv. machine. The original clinical classification was Stage II and the pathological Grade II. X-ray treatment was given through four lateral portals supplemented by an intravaginal port at the rate of 300 r. per day until a total of 21,000 r. was administered. This was followed by interstitial and intercavitary radiation equally divided for a total of 4,500 mg. hr. At the time of the node dissections performed 13 months thereafter little response to radiation was evident and both obturator areas contained large positive nodes. Within the past month this patient has developed a minor local recurrence at the apex of the vagina which is still pliable despite the intense radiation. A radical operation has recently been performed. It is now seven months since the node dissections were performed.

From the figures of the tabulation in Table IV, one might easily argue that much surgery is being done to recover relatively few positive nodes. Twenty-eight per cent were found to be diseased after complete radiation therapy. The series is too recent to refute the argument that surgery will not cure these patients any more than radiation will. On the other hand, Meigs has cured 30 per cent and Bomer 20 per cent where the nodes have been positive. Borrowing from the experience with cancer of the vulva where the same nodes may become involved, our experience confirms that of Taussig with 60 per cent surviving five years after radical dissection where positive nodes were found. Thus patients with diseased nodes have been salvaged by surgery.

TABLE IV

| | MASS. GENERAL (1,200 KV.) | PALMER (400 KV.) | PONDVILLE (200 KV.) | TOTAL | POSITIVE NODES |
|---|---|---|---|---|---|
| Total cases | 17 | 11 | 22 | 50 | |
| Positive nodes | 2 | 4 | 8 | 14 | 28 per cent |
| Mortality | 0 | 1 | 1 | 2 | 4 per cent |

Of the fourteen cases found to have positive nodes at the time of the dissection, four have died of distant metastases (two at 3 years and two at 10 months). Three of these had an original classification of Stage III. All recurred locally. In fact, four of the six patients with Stage III lesions had recurrence locally, evidence that the primary disease was not controlled. The one remaining case with a clinical classification of Stage III died at three years with local recurrence as well as distant metastases.

Three more patients have died, one succumbed to bronchopneumonia 5 months after operation; one died of pulmonary embolism 3 days post surgery, while the third developed an independent carcinoma of the colon with metastases from this alone.

TABLE V

| | MASS. GENERAL | PALMER | PONDVILLE | TOTAL | POSITIVE NODES |
|---|---|---|---|---|---|
| Stage I | 1 | 1 | 1 | 3 | 0 |
| Stage II | 16 | 8 | 17 | 41 | 20 per cent |
| Stage III | 1 | 1 | 4 | 6 | 67 per cent |

There remain eight cases of a total of fourteen which had regional node involvement on which to base the evaluation of this procedure as to the efficacy of surgery in the cure of nodes involved with disease.

As to the value of the surgical adjunct in the treatment of cancer of the cervix, time alone will produce the answer. To date only six patients have died of the whole group of fifty.

| | 1944 | 1945 | 1946 | 1947 | 1948 |
|---|---|---|---|---|---|
| Total | 6 | 7 | 24 | 11 | 2 |
| With nodes | 2 | 2 | 6 | 3 | 1 |

The numbers are too small and the series too recent to offer further observations.

## Conclusion

1. A simple surgical procedure has been added to the armamentarium of treatment of cancer of the cervix as a supplement to the radiation therapy.

2. While the immediate results are encouraging, the procedure of retroperitoneal node dissection following complete radiation therapy must be considered experimental.

## Discussion

DR. BAYARD CARTER, Durham, N. C.—The authors of this paper have presented an interesting survey. They stress the fact that the work is experimental.

The paper should be read by all interested in the treatment of cancer of the cervix whether their treatment is by irradiation, surgery, or a combination of irradiation and surgery.

The paper gives a good review of the results obtained by treatment with radium and x-ray. It stresses the fact that survival statistics have reached a plateau and calls attention to the fact that many of the patients who die from cancer of the cervix die with the disease sharply confined to the pelvis. It also recognizes the changes and improvement in radiation therapy and it poses the question of the highly controversial argument as to the effectiveness of x-ray therapy in curing the cancer in the nodes in the obturator, hypogastric, and iliac regions. The fact that there has been cancer extension in the pelvis before the patient is first seen is stated and with this statement we are in full accord. We also like the comparison drawn between carcinoma of the lip, tongue, and breast in the manifestations of its spread and carcinoma of the cervix and its extension.

Their description of the operation is excellent and they emphasize that the extra-abdominal approach of this operation permits wider applicability than does the intra-abdominal approach in the surgical treatment of cancer of the cervix.

One part of the paper was of singular interest to me. That part concerns the statement that preliminary x-ray therapy varied widely both as to voltage and dosage. In one institution a 1,200 kv. machine was used, whereas in two other hospitals 400 kv. and 200 kv. therapy units were used.

With this difference in therapy units and varied dosage the opportunity for study of the effect of radiation therapy on the metastatic carcinoma in the glands would be excellent. Of seventeen patients treated with the 1,200 kv. unit two had positive nodes; of eleven patients treated with the 400 kv. unit four had positive nodes; of twenty-two treated with the 200 kv. unit eight had positive nodes. Our hope is that the effect of the therapy on the cancer in the nodes may be explained in full and shown in slides.

Our experience with extraperitoneal (or extra-abdominal) lymphadenectomy has been limited entirely to those patients who had the operation performed as part of the treatment for vulvar squamous celled carcinoma.

Our reason for not doing extraperitoneal pelvic lymphadenectomy in treating post-irradiated squamous celled or adenocarcinoma of the cervix or of the cervical stump is based on the fact that in our first 75 patients treated by the Wertheim hysterectomy and radical pelvic lymphadenectomy we found:

a. Two patients, who had had full preoperative x-ray and radium therapy, with cancer still present in the cervix.

b. Three patients who had had preoperative x-ray therapy alone, with cancer in the cervix.

c. Three patients, who had had full preoperative x-ray and radium therapy, with what was described by the pathologist as "post-radiation" cancer of the cervix.

d. Two patients, who had not only metastatic cancer in the pelvic nodes but cancer still present in the cervix.

e. Three patients, who had not only "postradiation" cancer in lymph nodes, but cancer still present in the cervix.

We do the Wertheim hysterectomy and the radical intra-abdominal pelvic lymphadenectomy because we are afraid to leave the cervix and the parametrial tissues.

DR. FRANK R. SMITH, New York, N. Y.—I am glad to hear the speaker state that the work is experimental and not a proved method to turn loose on the public. At the Memorial Hospital we are using this method, although we are using radical lymph with total extirpation of genital organs more frequently. The last four of these patients upon whom I did extraperitoneal dissections had large nodes which proved to be benign. However, in this enthusiasm [and at Memorial we are treating all of our patients with cancer of the cervix by surgery now] I think we must, after an adequate length of time (by an adequate time, I mean at least five years), ask ourselves, Are we getting any salvage from the Stage IV group, are they living longer than they did under radiation, and are they more comfortable during their lives? Dr. Parsons and Dr. Meigs told me they had planned but had not carried out a program in which a psychiatrist would examine the patient before operation and then a few months afterward so that they would have an unbiased opinion as to whether the patient thought she was better off and it would not be the effect of a physician with a forceful personality turning on his charm. I think until we can answer these questions we do not have the answer as to the proof of this experiment.

DR. HERBERT E. SCHMITZ, Chicago, Ill.—One of the things your Cancer Committee had in mind when we submitted our report today was that we would have a yearly report from individuals or clinics relative to treatment of certain types of cancer found in the pelvis. I believe this would be of extreme value as each year we could have read within the report of the Cancer Committee the interreports of Dr. Meigs, Dr. Parsons and others working in the field of pelvic cancer.

Our first experience with metastatic lymph nodes came about some fifteen years ago when we attempted extraperitoneal ligation of the internal iliacs to see what effect that might have on the growth of the malignancy in the uterus, whether it would influence the spread of the disease or the reaction of the disease to irradiation. At that time we removed glands encountered in this area for microscopic section because they were easily accessible at that time. We have in that group a number who have returned with extension of the disease to

the cervical glands and some of these lived on another three or four years, and another into the fifth year. We know that there was a widespread dissemination of the disease throughout the lymphatic chain of these individuals, and I do not believe that the resection of the glands at that time contributed a thing.

The other question is the effect of irradiation on the lymph nodes or on the spread of the disease. I think we oftentimes overlook the actual effect of irradiation on malignant cells and the fibrosis which we produce with irradiation. This fibrosis entraps malignant cells and holds them at times for many years. If malignant cells were not entrapped by this means we would not have five-, ten-, or fifteen-year recurrence after irradiation. Surgery importunately used breaks down the fibrosis and some of these cells are free and the patient suffers a recurrence at a much earlier period.

The other thing is that we have found brain, osteogenic, and axillary gland metastasis from squamous cell cervical cancer years following primary treatment of the lesion. At autopsy there was no residual disease demonstrable in the pelvis proved by microscopic sections. This shows that there were distant lymph nodes invaded by tumor cells at the time of original therapy, and I am quite sure that eradication of the lymph nodes of the pelvis of these individuals would not have helped them in the least.

DR. J. W. KENNEDY, Philadelphia, Pa.—Within the hour I have been asked what would happen if Dr. Meigs, Dr. Cashman, and I were working in the same clinic. Probably it has been within the last ten seconds that the meaning of this inquiry has come to me. The physician who asked this question knows of Dr. Meigs' classical hysterectomy from above, he also knows of Dr. Cashman's attempts at prevention of malignancy of the cervix by the use of the cautery, and further evidently knows that I once in a while perform vaginal hysterectomy by clamp method for early malignancy of the uterus. Well, what would probably occur? I am sure we would continue to speak to each other and that Dr. Meigs would soon entice me to make an attempt to perform his radical abdominal hysterectomy, and that under an act of legerdemain I might persuade Dr. Meigs to try a vaginal hysterectomy or two by clamp method for early malignancy and then Dr. Cashman would take the wind out of our sails by saying, "Why are you working so hard from above and below the pubic arch in your fight against uterine malignancy; why not prevent the same by the prophylactic use of the cautery?" and would then tell us of a long series of cases, several thousand, in which the occurrence of malignancy of the cervix following his use of the cautery was practically nil. Does this not mean we all have something of worth and that we must segregate our knowledge as would occur among honest men intimately associated.

Throughout the life history of the Joseph Price Hospital there has not been a case of malignancy of the cervix following our repairs of that structure. It is difficult to interest the profession in the simple things such as that of repair of the cervix or any simple method of restoring the cervix to its natural outline and healthy structure which would prevent over ninety per cent of the malignancies of the uterus; this seems to be so simple that it is not even interesting.

We have said elsewhere in literature that plastic surgery (repair of the cervix and repair of the perineum) is a lost art. We never use any kind of absorbable sutures in our vaginal surgery. We use silkworm-gut which has all the stable qualities of Marion Sims' silver wire or Babcock stainless wire. All of our sutures in the cervix or perineum are mass sutures. We never use the terrace method of suturing in vaginal surgery.

It is next to impossible to infect the mass suture. It is in itself a drain. The repairs of the cervix as too often illustrated are too superficial in extent of tissue removed to be of any service from the standpoint of malignancy prevention or of restoration of the structure to its normal outline and relations.

In the bilateral tear of the cervix deep plugs of tissue including the entire thickness of the cervix are removed. This will leave a very small portion of the mucous membrane of the endocervix which is curetted by a sharp bone curette.

We take the position there is no organ in male or female where prophylactic surgery can be demonstrated to be of such sterling worth in prevention of malignancy in over 90 per cent of the cases as in repair of the cervix.

For this reason we take the position that the greatest example of a therapeutic anachronism of which we have knowledge is our failure to clean up the cervix by returning it to its normal outline and relations as a preventive source of cervical malignancy.

In closing, I say we are still ploughing our ground with crooked sticks as far as the treatment of malignancy of the uterus is concerned.

DR. LANGDON PARSONS, Boston, Mass. (Closing).—It is obvious that one cannot evaluate the efficacy of radiation in the treatment of nodes involved in disease from carcinoma of the cervix on the basis of fifty cases. Certain observations have become apparent in this study to cast a serious cloud of doubt, however. This series is of too short duration to give much of an indication as to whether surgery will prove any more successful than radiation in the salvage of cases where the nodes are involved.

It is perhaps too much to ask of x-ray to deliver a cancerocidal dose to the extensive area of potential disease encountered in cancer of the cervix without running the risk of damage to viscera such as bladder and bowel. A photomicrograph is presented bearing on this point. Here a 400 kv. machine had delivered 7,200 r. measured in air through four portals. Following interstitial and intercavitary radiation in dosage of 4,500 mg. hr. total, dissection of the nodes was undertaken four months later. The slide certainly suggests that the positive node encountered along the common iliac was completely outside the field of radiation for normal fat, open sinusoids, and unaltered gland structure are present. Progressing into the field of radiation the nodes show partial replacement by fibrosis but large areas of tumor cells apparently undamaged. Whether these cells are biologically active cannot be determined but in the opinion of Dr. Shields Warren, microscopically, at least, the tumor cell has been unaffected by the radiation.

A certain photomicrograph presented shows extensive radiation reaction in the node found in the internal iliac area in keeping with the extreme degree of stromal reaction encountered surgically. Again untouched but obviously encapsulated tumor cells are found. Perhaps this is what radiation is meant to do but perhaps also this may in part explain the late recurrences occasionally encountered.

The extent of the radiation and the grade of the tumor would seem to be of no help in anticipation of the effect of radiation. 16,000 r. measured in air with a 200 kv. machine had little effect on the nodes involved by adenocarcinoma of the cervix. The stromal reaction was extreme but neither the uninvolved or the diseased nodes show any sign of radiation reaction.

A further case proved instructive as well as encouraging, for after 21,000 r. delivered by 200 kv. through four lateral and one intravaginal portal, followed by 4,500 mg. hr., large masses of positive nodes were found 13 months later when node dissections were done. Despite the extent of radiation the surgery was easily accomplished and evidence of radiation reaction, as indicated by the mobility of the bladder and the pelvic floor, was completely lacking. Eight months later, or 29 months post radiation, the vaginal smear noted recurrent local disease confirmed by biopsy. A Wertheim procedure was then carried out with ease despite the amount of radiation. The encouraging note appeared when no obvious disease could be found in the nodes along the cortex or in the areas previously operated upon where extensive disease had been present.

DR. FREDERICK H. FALLS, Chicago, Ill.—I would like to ask Dr. Meigs what he thinks the action of x-ray and radium on the cells that are not in the lymph glands might be? He routinely takes out all the palpable lymph nodes invaded by cancer cells. However, the intercommunicating lymphatics are still present. Does he think that the carcinoma cells in the lymph channels via these lymphatics are particularly vulnerable to x-ray and radium?

DR. MEIGS (Closing).—I am sorry, Dr. Falls, I do not know the answer to your question. I know that we do find cancer in the parametrium, in which the lymphatics run, but whether it runs in continuity up the chain, I do not know.

I do think we should at least try this method out before we say that surgery is of no value in the treatment of cancer of the cervix.

# AN ATTACK UPON THE DELAY PERIOD IN DIAGNOSIS OF PELVIC CANCER*

## With Further Observation of the Philadelphia Study

JOHN Y. HOWSON, M.D., AND THADDEUS L. MONTGOMERY, M.D.,
PHILADELPHIA, PA.

FOUR years ago, when a Cancer Committee of this Association was appointed, it was proposed that one of its activities might be the encouragement of a study of cancer deaths in local communities along the same lines which had been laid down in the study of maternal mortality.

This proposal was taken back to Philadelphia and placed before the Obstetrical Society of Philadelphia, the local chapter of the American Cancer Society, and the Philadelphia County Medical Society. These organizations approved of the idea and with the cooperation and support of the Department of Public Health of Philadelphia underwrote the project successively for these past three years. Funds for the study were provided by the American Cancer Society.

Accordingly, it seemed pertinent to report back to this parent organization on the progress of an undertaking which was first suggested here, and to consider the significance of some of the procedures, particularly as they have had to do with a general attack upon the delay period in the diagnosis of cancer.

The accompanying report is a résumé of the first 1,140 cases analyzed. There are some statistical data which will be presented; however, the most important consideration of the paper appears to the authors to be the educational value of a program in which general practitioner, public health officer, and gynecologist participate, and in which are brought to light the numerous problems which arise in pelvic cancer diagnosis in the practice of the family or community doctor. These problems are often too little appreciated or understood by the specialist.

Several reports concerning the organization of the early work of the Philadelphia Study of Pelvic Cancer have been presented by the Chairman of the Committee, John Y. Howson.[1, 2] This material does not need to be repeated except to state for the purposes of this presentation that while studies were first started with the analysis of cases in which the patients had died, as is the custom in the Maternal Welfare analyses, a change was soon made to the consideration of active patients registered in the tumor clinics of the city, so that the details of diagnosis and management would be fresh in mind.

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Thus far the study has been limited to patients who appear in the various hospital clinics of the city and who constitute the ward or "charity" group. In the fall it is planned to extend the analysis to private and semiprivate patients.

Meetings are open to all interested physicians. Those doctors who are concerned in the delay period of cases presented for discussion are individually invited by letter and telephone. Their response has been gratifying. In addition, there have regularly been present gynecologists from the hospitals and teaching institutions of the city, residents and interns, and many other physicians from Philadelphia and neighboring cities.

The attendance, the enthusiasm, and the degree of participation of these various groups has increased progressively; all apparently look forward to this meeting as one of the important educational experiences of the month.

In presenting these data the essayists desire to emphasize these are not figures collected from hospital records. Rather, they are the account of experiences which have been secured by the committee secretaries from the patients themselves. A decision as to whether there has been physician delay has been reached by the committee in open session. At this session the physicians involved have presented their point of view in each case. Therefore, the facts that are presented in these charts, and the conclusions which may be drawn therefrom have already been indelibly impressed on the minds of those with whom the patient first made contact.

As to the data themselves, they confirm the universally recognized and lamented fact of lost time between the appearance of symptoms and the establishment of diagnosis. In this study delay has been presumed to exist on the patient's part if more than one month elapsed between the appearance of symptoms and the securing of medical opinion. Delay is assumed to exist on the physician's part if more than one month elapsed between the first visit of the patient and the establishment of a diagnosis. On this basis there were only 28.2 per cent of cases in which there was no delay (Table I). The total patient delay was 56.9 per cent, and the total physician delay was half of that or 27.7 per cent.

TABLE I. PROPORTIONS OF PATIENT AND PHYSICIAN DELAY IN 1,140 CASES INVESTIGATED AS OF JULY 1, 1948

| | NUMBER | PER CENT |
|---|---|---|
| Patient delay | 502 | 44.0 |
| Physician delay | 169 | 14.9 |
| Physician and patient delay | 147 | 12.9 |
| No delay | 322 | 28.2 |
| Combined patient delay | 502 plus 147 | 56.9 |
| Combined physician delay | 169 plus 147 | 27.7 |

In a consideration of delay by organs involved, or site of cancer (Table II), it is to be noted that there was the highest percentage of patient delay in the case of cancer of the vulva, and the highest percentage of physician delay in cancer of the ovary and cancer of the vulva. In both of these latter sites the failure to examine rate on the part of the physician was extremely high, 62 per cent and 71 per cent, respectively (Table IV).

TABLE II. DELAY BY ORGANS OR SITE

| | CERVIX | FUNDUS | OVARY | VULVA |
|---|---|---|---|---|
| Total number cases | 718 | 259 | 86 | 22 |
| No delay | 30.5% | 23.5% | 22.1% | 13.6% |
| Patient delay | 56.8% | 59.8% | 57.0% | 72.7% |
| Physician delay | 24.5% | 28.5% | 43.0% | 36.4% |

The average duration of physician delay, as illustrated in Table III, varies from 7.4 months in the case of cervical cancer to 19.0 months in cancer of the vulva. Table IV presents the tremendous part that failure to examine played in the failure to diagnosis cancer in four common sites, ranging from 48.6 per cent in the case of fundus of the uterus to 71.2 per cent in the relatively few cases of cancer of the vulva. The old medical adage that more mistakes are made by failure to look than by failure of knowledge seems well supported by these observations. Table IV also enumerates the number of physicians involved in failure to examine, there being in some cases two to five physicians.

TABLE III. AVERAGE LENGTH OF PHYSICIAN DELAY

| | |
|---|---|
| Cervix | 7.4 months |
| Fundus | 13.7 months |
| Ovary | 9.6 months |
| Vulva | 19.0 months |

TABLE IV. DELAY IN DIAGNOSIS DUE TO FAILURE TO EXAMINE PATIENT

| ORGAN | PHYSICIAN DELAY | NOT EXAMINED | NUMBER OF PHYSICIANS INVOLVED |
|---|---|---|---|
| Fundus | 74 | 36—48.6% | 90 |
| Cervix | 178 | 92—51.1% | 203 |
| Ovary | 37 | 23—62.1% | 45 |
| Vulva | 7 | 5—71.2% | 8 |

The reasons for physician delay and the treatments that were given upon the basis of no specific diagnosis or a wrong diagnosis are enumerated in Table V. In 49.3 per cent of the total cases of physician delay no local examination was made. In 48.7 per cent an examination was made but a wrong diagnosis was established. Many forms of treatment were prescribed for this unfortunate group of patients, of which the most common was the oral or hypodermic administration of "hormones."

TABLE V. REASONS FOR PHYSICIAN DELAY AND TREATMENTS EMPLOYED

| | |
|---|---|
| No examination made | 156 or 49.3% |
| Examination made—wrong diagnosis | 154 or 48.7% |
| Oral medication, needles or both | 112 |
| Local treatment of cervix | 26 |
| Douches | 24 |
| Told it was menopause | 23 |
| Diathermy | 4 |
| Rest | 4 |
| Examination deferred until bleeding stopped | 9 |
| Examination to be made if bleeding recurred | 3 |

Not all of these instances of physician delay occurred among general practitioners. There were 28 cases in which delay in either diagnosis or treatment occurred on the services of Philadelphia hospitals. Time does not permit of the enumeration of all the causes of delay in this group of patients;

however, it is interesting to note that one of the very common causes was the performance of inadequate surgery before the presence of carcinoma had been ruled out by appropriate study.

Table VI presents a comparison of our figures with those collected by Pack and Gallo[3] at Memorial Hospital in 1938, and Leach and Robbins[4] at the same institution in 1947.

TABLE VI. COMPARISON OF STUDIES

| | PACK AND GALLO (1938) (PER CENT) | LEACH AND ROBBINS (1947) (PER CENT) | HOWSON AND MONTGOMERY (1948) (PER CENT) |
|---|---|---|---|
| Patient delay | 44.3 | 32.0 | 44.0 |
| Physician delay | 17.0 | 10.8 | 14.9 |
| Patient and physician delay | 18.0 | 27.8 | 12.9 |
| No delay | 20.7 | 29.4 | 28.2 |
| Total physician delay | 35.0 | 36.6 | 27.7 |

## Discussion

These figures and tables all indicate that if a full front attack is to be made upon the cancer problem the patient must be brought to the doctor at an early date and the doctor must use all available means to establish an early and accurate diagnosis. The weak spot remaining in the offense against cancer is the period before therapy.

The American Cancer Institute and other similar organizations are not unmindful of this fact.[5] While large sums of money are being spent for cancer research, sizable amounts are being expended also upon education.[6] The Public Health Service has set aside funds for the subsidizing of chairs of oncology in the medical schools of the country,[6] and enhancement of the teaching of undergraduate students in this field is urged.[5] Cancer detection clinics are appearing in large and small communities.[7, 8, 9, 10] Medical societies bristle with papers on cancer diagnosis and therapy. With it all there is a great deal of talking *at* the physician who is out on the frontier zone of family practice, but not much talking *with* him.

One is reminded of a similar situation that existed twenty years ago in reference to maternal mortality. Maternal death rate was high, everyone knew it was high, and innumerable hospital reports re-emphasized the fact. Civic, state, and national lay organizations united in an attack upon the deplorable situation. But nothing happened until a small group of courageous obstetricians in New York and Philadelphia started the investigation of maternal deaths and called in for discussion the physician connected with each case. When this movement established itself and spread throughout the United States the rates of maternal death began to fall so that this country now enjoys an enviable reputation in the field of Maternal Welfare.

On the basis of its first three years of activity the Philadelphia Committee on Pelvic Cancer is convinced that a situation similar to the maternal mortality problem exists in the delay period of cancer diagnosis and that the situation will not soon be corrected until physicians sit down with physician and endeavor to clear the house in cancer diagnosis delay.

Just how important these conferences may be are revealed in the many reasons for delay in diagnosis which have been presented and discussed before the committee. It is worth while recording a few of them:

1. Reluctance to perform pelvic examination when a patient is bleeding.
2. Confusion as to what constitutes a normal menopause and what is a significant departure from normal.
3. Difference of opinion as to the minimum requirement for handling correctly the patient with minimal abnormal menopausal symptoms.
4. Indecision as to whether a pelvic examination should be made in the home or whether a chance of delay may be incurred by postponing examination until the patient can appear at the office.
5. Failure to follow up the patient with suggestive symptoms, and lack of appreciation of the minimum requirements for keeping patients under observation.
6. Question as to whether all erosions of the cervix should be biopsied.
7. Difference of opinion as to whether tissue should be obtained from the cervix and uterus in the doctor's office, and if so, by what method.
8. Lack of equipment and facilities in many general practitioners' offices for the convenient performance of pelvic examination.
9. Lack of "time" for complete examination and pelvic study during office hours.
10. Failure to incorporate pelvic examination in the physical examination of patients with obscure lower abdombinal symptoms.
11. Confusion between general practitioners and gynecologist as to who shall follow up patients after radiologic treatment.
12. Unsettled opinion as to the place and applicability of the Papanicolaou smear in the office diagnosis of uterine cancer.
13. Fear on the part of the general physician that the urging of pelvic examination will create an undesirable reaction in his clientele and turn patients away.
14. Special problems involved in the diagnosis of uterine cancer in virgins and nulliparous old patients.
15. Question as to the safety of sounding the uterine cavity in the office.
16. Failure to perform a pelvic examination at patient's first visit.
17. Indiscriminate use of hormones as a substitute for accurate diagnosis.
18. The menace of the statement, "No need to worry about irregular periods in the forties; you are probably changing life."
19. Assumption that such obvious pathology as senile vaginitis, polyps of cervix, etc., are the sole cause of irregular bleeding.
20. Delay in the admission of some cancer patients because of the shortage of hospital beds.
21. Placing too much reliance on the findings of pelvic examination made by young members of the hospital staff and by residents in training.
22. Failing to rule out the possibility of uterine cancer before operating for uterine myomas and other pelvic lesions.

The answers to some of these problems seem sufficiently obvious to require no further comment, and doubtless many physicians left the conference meetings with the decision that they must either better equip themselves to diagnose pelvic cancer or send the patients to someone else. In other cases the questions have brought out numerous difficult and unsolved matters any one of which might constitute the subject of more detailed consideration. In either case the problems of general practice were brought out and the doctor and the committee came to grips with them and probably none of those present will forget the discussions which arose. The family physician has

taken away an indelible impression of his importance in early diagnosis, the gynecologist has had re-emphasized his grave responsibilities in treatment and follow-up, and the teacher has had pointed out to him the directions in which his instruction has fallen short of the mark.

As you may by this time have realized, the Committee for the Study of Pelvic Cancer in Philadelphia believes that this method of case study, essentially the same as was employed by the Philadelphia Maternal Welfare Committee, closes a wide gap in the attack upon the delay period in cancer diagnosis. While the progress may be slow, just as it was in the case of the Maternal Welfare program (Table VII), eventually the word will get about. It will become known that there is a substantial group of the profession who are bent upon seeing this thing through, and inexorably the weight of opinon will be felt in every office and clinic of Philadelphia. As the doctor examines his patient he will sense the presence of an invisible third person who is sympathetically but carefully watching the fashion in which he discharges a full duty to the cancer patient.

TABLE VII. LIVE BIRTHS AND MATERNAL DEATHS, PHILADELPHIA, 1931-1947
(SINCE THE INAUGURATION OF THE MATERNAL WELFARE COMMITTEE)

| YEAR | LIVE BIRTHS | MATERNAL DEATHS |
|---|---|---|
| 1931 | 33,773 | 6.00 per 1,000 |
| 1932 | 32,093 | 6.6 |
| 1933 | 29,528 | 4.6 |
| 1934 | 29,751 | 5.3 |
| 1935 | 29,988 | 4.9 |
| 1936 | 29,652 | 5.3 |
| 1937 | 30,059 | 3.9 |
| 1938 | 30,739 | 3.2 |
| 1939 | 30,232 | 2.8 |
| 1940 | 31,227 | 2.4 |
| 1941 | 34,118 | 2.6 |
| 1942 | 41,978 | 2.4 |
| 1943 | 43,521 | 2.3 |
| 1944 | 38,825 | 2.7 |
| 1945 | 38,899 | 2.1 |
| 1946 | 46,907 | 1.3 |
| 1947 | 52,932 | 1.4 |

## Summary

A report has been submitted from the Philadelphia Committee for the Study of Pelvic Cancer, describing its efforts to reduce the delay period in the diagnosis of pelvic cancer by a method of study similar to that employed for many years in Maternal Welfare circles.

Eleven hundred forty cases have been analyzed by personal interview with patients. In this group there was no delay of diagnosis in 28.2 per cent, a total patient delay of 56.9 per cent, and a total physician delay of 27.7 per cent.

When there was physician delay, the doctor concerned was invited to attend the meeting of the committee and discuss the obstacles he encountered in attempting to make a diagnosis.

Many reasons for physician delay have been come upon and recorded. These were freely discussed in open meeting and in each case an effort made to reach a solution.

On the basis of this experience the committeee desires to emphasize the educational value of a plan in which general practitioner and gynecologist discuss together their common problems. The concerted weight of physician opinion which becomes crystallized in this method of approach should become effective in reducing cancer delay diagnosis as it has been effective in the past in lowering maternal mortality.

## Acknowledgment

The authors call attention to and gratefully acknowledge the contribution which the physicians of Philadelphia and the members of the Committee for the Study of Pelvic Cancer have made to this subject matter. They trust that the point of view of these groups has been properly represented.

They are also indebted to Mrs. Ruth Behr and Miss Etta Jones, the secretaries of the Committee, for their assistance in collecting these data and their valued part in the long-term interests of this Philadelphia study.

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## Discussion

DR. R. E. CAMPBELL, Madison, Wis.—Dr. Montgomery and his co-workers have organized and coordinated with the several societies in Philadelphia an investigation which has resulted in a productive approach and inestimable cooperative effort in the field of cancer. It is refreshing to note that criticism has been constructive and not destructive and that the investigative effort has not produced animosity but good will and support by the community or family doctor. I emphasize again that which has been brought out so forcibly by the essayists that the physician who is out on the frontier zone has been talked *with* and not *at*.

The American Association of Obstetricians, Gynecologists and Abdominal Surgeons can be proud of this monumental and fearless report just presented. The Association is also indebted to those organizations in Philadelphia which have helped to make this investigation possible. This study has not only an important investigative value but its invaluable educational aspects are of extreme import not only in postgraduate medical education but in teaching of medical students, interns, and resident physicians.

It is highly significant that the investigation has been made not from the records of dead patients but from personal reports of living patients and their physicians who gave accurate information.

It is not within my province to discuss in the time allotted to me this important report. However, I wish further to comment on, and to re-emphasize, some of its most important findings.

The patient and physician delay in 1,140 cases as presented in this report in Table I of 56 and 27 per cent, respectively, and no delay in diagnosis in only 28.2 per cent of these cases is amazing to some of you but should be shocking to all of us. Now, combine the foregoing failure of physicians to examine their patients—pardon my repetition and the re-emphasizing of Table IV which shows a delay in diagnosis due to failure to examine the patient with figures of 48.6 per cent in fundal cancer, 51.1 per cent in cervical cancer, and a high of 71.2 per cent in vulvar cancer—then you must conclude that such a situation is reprehensible. In addition, add to this lamentable situation the figure 48.7 per cent in wrong diagnosis as shown for physician delay in Table V and substitutional therapies such as endocrine therapy, cauterization, diathermy, douches, etc., then you have a composite story which is tragic.

I know that the same problems relative to cancer diagnosis exist in Madison as in Philadelphia and am reasonably certain that they exist in Chicago, Indianapolis, New York, and other metropolitan as well as rural centers.

In conclusion, I am sure that cancer diagnosis can and will be improved in a similar approach to that employed by the Maternal Welfare Committees in Obstetrics; however, it must be a frontal attack with a determined effort to carry any such plan through. The Philadelphia Cancer Committee has shown us the way. Women must have more information on cancer and both undergraduate and postgraduate medical teaching relative to it must be improved and extended.

DR. CLAYTON T. BEECHAM, Philadelphia, Pa.—The work of the "Committee for the Study of Pelvic Cancer" in Philadelphia has been well documented by the authors. It is too early for an appraisal of the over-all effect this investigation has on medical practice in Philadelphia County. However, we have observed an improved conduct in regard to malignancies by general practitioners who refer work into the clinic at Temple University. We believe this improvement is due in part to some of the doctors having appeared before the committee in regard to their patients, and the monthly summary of meetings published by the County Medical Society.

We owe much to Dr. Montgomery for his initiative in the Cancer Committee of this Association and for being the initiating force in Philadelphia for organizing the "Study Committee" through the Philadelphia Obstetrical Society. His participation has been most helpful and active.

The work of the committee has only begun. Continued improvement is to be looked for in shortening the delay period. Other problems in diagnosis and management of pelvic cancer will we hope be increasingly dealt with as time goes on.

DR. HARVEY B. MATTHEWS, Brooklyn, N. Y.—Judging from this masterful presentation by Dr. Montgomery it is clear that we need more and better education among the doctors on the problem of cancer. Since 1913 we have had in New York City considerable and widespread education of the public by the American Cancer Society and its associated agencies, which we believe has been fairly adequate. The public response is increasing day by day. On the other hand, it appears that the education of the doctors has definitely fallen short of its rightful goal. This simply means that the medical schools and hospitals, but particularly the medical schools, have not measured up to their duties in teaching cancer to undergraduate and postgraduate students. It would, therefore, seem to me that from now on we should encourage more and better "cancer" teaching for the doctors. I know of but two or three medical schools in the country where adequate instruction in cancer is given to undergraduates. In my own medical school we have been able to give only two or three didactic lectures with very little clinical demonstration on cancer in the female. In consequence I feel that we have fallen short in the instruction of our students in relation to the cancer problem. I am sure that with very few exceptions this same condition exists in other medical schools (and hospitals) throughout the country. It would seem to me, in view of the present-day

inadequacies in our teaching institutions, that this organization could "cut a wide swath" in respect to better cancer instruction in our medical schools and hospitals, because so many of you are members of the faculty and/or directors of services in your respective institutions and hence have it within your power—each of you—to provide more and better facilities for teaching this important subject. The American Cancer Society is doing an excellent job in educating the public; the medical schools should be doing a better job instructing the doctors.

DR. EMIL NOVAK, Baltimore, Md.—The literature for years has teemed with papers on the surgical and radiologic plans of treating uterine cancer, and the net result in lives saved by improvements in both methods has been well worth while, but scarcely impressive. The simple paper we have just heard, dealing with efforts at unearthing cancer in its early and favorable stages, points the way to a wide-open avenue for the saving of many more human lives than are likely to be saved from any surgical or radiotherapeutic improvements in the foreseeable future.

DR. JOHN Y. HOWSON, Philadelphia, Pa.—There are just two points I would like to emphasize about the work under discussion. The first is the enthusiasm we have for this undertaking in Philadelphia, and how anxious we are that you physicians will at least grasp some of this enthusiasm and take it back to your communities where, perhaps, the same type of work can be initiated. Perhaps ultimately we can hope for success comparable to that of the Maternal Welfare activities.

The second point is that the significance of this work lies in the fact that we feel we are reaching the one who needs the education most. The busy physician has all too little time to attend meetings, to read the literature, and to keep up with the modern concepts and practice of medicine. By reaching directly those doctors who see the patients first, and who are responsible for their ultimate care, we feel we are contributing something of practical value to this problem of early cancer diagnosis.

DR. MONTGOMERY (Closing).—I would like at this time to repeat that what progress has been made in collecting and analyzing this data and in advancing the interests of cancer diagnosis in Philadelphia is a cooperative effort in which the physicians of Philadelphia themselves have played a major part.

# CLINICAL AND PATHOLOGICAL STUDIES OF FEMINIZING TUMORS OF THE OVARY*

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WHEN a new form of tumor is discovered and described, in most cases it is brought to the attention of the medical profession by men interested in the pathology of the tumor. Its histopathology is described and soon it becomes recognized as an entity. Next follows an awakened interest in the clinicians to arrive at a diagnosis preoperatively, based on clinical manifestations or physical peculiarities. The most important feature of most ovarian neoplasms clinically is whether or not they become malignant, and if so what proportion undergo such changes and how may this tendency be detected. Because of the limited experience of any one clinician or pathologist with these tumors, careful study and analysis and classification of these tumors is considered of great importance. Even with a large series of ovarian tumors such as is here presented the number of feminizing tumors is so small that the percentage figures here given are obviously of little statistical significance except to add to a sufficient number of other series so that the final figure could be so considered.

Dockerty and McCarty[1] in 1939 reported 300 cases in the literature. Since then, Dockerty[2] in his collective review of the recent literature has shown that the number of cases reported has doubled. The increased recognition of feminizing tumors in the ovary was chiefly due to the impetus given to this study by the work of Meyer,[3] Schiller,[4] Novak[5] and others who have contributed to our knowledge of the anatomy, histopathology, and abnormal physiology of these feminizing tumors of the ovary.

Of the feminizing tumors, the granulosa cell tumor was first described by Von Kahlden[6] in 1895, but it was not until 1914 that Van Werdt[7] applied to the tumor its present name. Theca cell tumors were first described by Loeffler and Priesel,[8] using the terminology zanthofibroma theca-cellulare.

## Material

We have had the opportunity to review the feminizing ovarian tumors in the surgical material at Cook County Hospital collected during the past fourteen and one-half years, from July, 1931, through December, 1946. A total of 1,622 tumors of the ovary, either solid or cystic, were examined. Of these, 59, or 3.6 per cent, were feminizing tumors, the granulosa cell group comprising 1.78 per cent and the theca cell group 1.82 per cent. The per-

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centage of granulosa cell tumors in this series of cases parallels the series reported by Fauvet[9]; but is twice the number described by Szathmary.[10] Spencer and Hollenbeck[11] in their series of 208 ovarian neoplasms found five cases of granulosa cell tumors (2.4 per cent). Of the granulosa cell tumors in our series, nine, or 31 per cent, were malignant. This percentage corresponds closely with that given by Novak.[12]

As indicated above, the incidence of theca and granulosa cell tumors was found to be almost equal. This is at variance with the statistics of Banner and Dockerty[13] who find theca cell tumors one-half as common as granulosa cell tumors of the ovary.

Of our 59 cases, complete clinical data and pathological material were available for 39 cases, and our analysis will be based on these. The incidence of granulosa cell tumor was 59 per cent and that of theca cell tumor 41 per cent.

The age distribution in our series varies from 20 to 71 years in the granulosa cell tumors (Table I) and from 23 to 64 years of age in the theca cell tumors (Table II). The average age was 45 years in the granulosa cell tumor series and 44.6 years in the theca cell tumors. Granulosa or theca cell tumors were not found in the prepubertal age in our series.

TABLE I. DISTRIBUTION OF GRANULOSA CELL TUMORS AS TO AGE AND RACE

| AGE IN YEARS | RACE | | BENIGN | | MALIGNANT | | PER CENT IN DECADES | |
|---|---|---|---|---|---|---|---|---|
| | W | N | W | N | W | N | W | N |
| 1-9 | – | – | – | – | – | – | – | – |
| 10-19 | – | – | – | – | – | – | – | – |
| 20-29 | 2 | – | 2 | – | – | – | 8.7 | – |
| 30-39 | 1 | 3 | 1 | 2 | – | 1 | 4.3 | 13.0 |
| 40-49 | 2 | 8 | 1 | 4 | 1 | 4 | 8.7 | 34.7 |
| 50-59 | 2 | 2 | 1 | 1 | 1 | 1 | 8.7 | 8.7 |
| 60-69 | 1 | 1 | 1 | 1 | – | – | 4.3 | 4.3 |
| 70-79 | 1 | – | 1 | – | – | – | 4.3 | – |
| Total | 9 | 14 | 7 | 8 | 2 | 6 | | |
| Per cent as to race | 39.1 | 60.9 | 30.4 | 34.7 | 8.7 | 26.1 | | |

TABLE II. DISTRIBUTION OF THECA CELL TUMORS AS TO AGE AND RACE

| AGE IN YEARS | RACE | | BENIGN | | MALIGNANT | | PER CENT IN DECADES | |
|---|---|---|---|---|---|---|---|---|
| | W | N | W | N | W | N | W | N |
| 1-9 | – | – | – | – | – | – | – | – |
| 10-19 | – | – | – | – | – | – | – | – |
| 20-29 | – | 2 | – | 2 | – | – | – | 12.5 |
| 30-39 | 2 | 1 | 2 | 1 | – | – | 12.5 | 6.25 |
| 40-49 | – | 4 | – | 4 | – | – | – | 25.00 |
| 50-59 | 1 | 5 | 1 | 5 | – | – | 6.25 | 31.25 |
| 60-69 | – | 1 | – | 1 | – | – | – | 6.25 |
| 70-79 | – | – | – | – | – | – | – | – |
| Total | 3 | 13 | 3 | 13 | | | | |
| Per cent as to race | 18.7 | 82.3 | 18.7 | 82.3 | | | | |

In the granulosa cell group, 60.8 per cent occurred in the reproductive period and 39.2 per cent in the postmenopausal group. This is in general agreement with the findings of Dockerty,[2] with the exception that in the prepubertal group we found none as compared to the incidences of 5 to 10 per

cent recorded in the literature. In the theca cell group, 56.2 per cent were found in the reproductive period and 43.8 per cent in the postclimacteric period. This finding is at marked variance with the findings of Banner and Dockerty,[13] who have recorded only 35 per cent before the age of 50. Regarding the average age in the malignant granulosa cell tumor group, there was a range from 32 to 54 years with an average of 43.4 years. Only one case of malignant granulosa cell tumor was noted before the fourth decade (Table I). This emphasizes the need for more radical surgery in the older age group and the advisability of relative conservative management in the younger age group, as advocated by Dockerty.[2]

*Race.*—The distribution of feminizing tumors in white and Negro showed a rather unusual disproportion. The Negro patients had a considerably higher incidence than the white patients, especially in regard to theca cell tumor (Tables I and II). Our basis for comparison was the total admissions to the gynecological service over a nine-year period, during which time 17,560 patients were admitted. Of these, 42 per cent were of the white race and 58 per cent of the Negro race. It is felt that this gives a fair representation of the two races on the gynecological service. Of the total number of feminizing tumors, 69.23 per cent were found to be in women of the Negro race, whereas 30.77 per cent were found in the white race. Breaking down our findings of the theca and granulosa cell tumor groups in relation to the white and Negro races, the incidence in the granulosa cell group is 60.9 per cent of the Negro and 39.1 per cent of the white (Table I). In the theca cell group, 82.3 per cent occurred in the Negro race and 18.7 per cent in the white race (Table II). It is thus demonstrated that there is an increase, above the anticipated incidence, of feminizing tumors in the Negro race, this increase being 11.23 per cent in the feminizing tumors as a group. In the granulosa and theca cell tumors, there is an increase of 12.9 per cent and 24.3 per cent, respectively.

*Age.*—The age range among the Negro women in the theca cell group varied from 23 to 64 years with an average age of 45.61 years, whereas the white range was from 34 to 60 years and averaged 40.33 years. The age range of granulosa cell tumors in the Negro race varied from 33 to 66 years with an average of 45.5 years, whereas in the white race, in a series of 3 cases, the range was 36 to 54 years with an average of 43.3 years. As far as malignant granulosa cell tumors are concerned, six of the nine cases, or 66 per per cent, occurred in the Negro race, which parallels the incidence of granulosa cell tumor in the Negro and white race. These figures would seem to indicate that feminizing tumors are more frequently found in the Negro than in the white race, this increase being due chiefly to the large number of theca cell tumors in the Negro. This would correspond to other evidences of increased irritability of the fibroblastic cells in this race (fibroblastic diathesis). As to the age incidences in these tumors, no striking differences are noted in the average age between white and Negro except for the theca cell group.

*Menstrual History.*—One might expect to find in the menstrual history of these women that an appreciable difference would be noticed in the time of onset, amount, or character of the menses. Study of the histories in these 39 cases failed to reveal any evidence that the onset of this function was noticeably altered, or appeared earlier in these girls than in those who did not later develop feminizing tumors. The age at onset varied from 11 to 17 years.

*Feminizing Tumors in the Reproductive Period.*—There were 23 cases (Table III) of feminizing tumors in women of the reproductive period. Of these, 14 were of the granulosa cell and 9 were of the theca cell type. Five of the granulosa cell tumors were manifestly malignant by either clinical or histological evidence or both.

TABLE III. SUMMARY OF CLINICAL AND PATHOLOGICAL FINDINGS IN FEMINIZING TUMORS OF THE OVARY IN THE REPRODUCTIVE PERIOD

| RACE | AGE (YEARS) | THECA CELL TUMOR | GRANULOSA CELL TUMOR BENIGN | GRANULOSA CELL TUMOR MALIGNANT | DURATION OF MENSTRUAL DISTURBANCE | AMENORRHEA | MENORRHAGIA | METRORRHAGIA | AMENORRHEA FOLLOWED BY MENORRHAGIA OR METRORRHAGIA | PALPABLE ADNEXAL MASS | ATROPHIC ENDOMETRIUM | HYPERPLASTIC ENDOMETRIUM | UTERINE POLYPS | UTERINE FIBROIDS | CARCINOMA OF CORPUS | MEIGS' SYNDROME | COMMENTS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N | 23 | + | – | – | Years | – | – | + | – | + | ? | ? | ? | – | – | – | |
| N | 28 | + | – | – | 2 mon. | + | – | – | – | + | – | + | – | + | – | – | |
| N | 31 | + | – | – | None | – | – | – | – | + | – | + | – | + | – | – | |
| N | 32 | – | – | + | 2 mon. | + | – | – | – | + | ? | ? | ? | – | – | – | Menstruated regularly. |
| N | 33 | – | + | – | 10 years | + | – | + | + | + | ? | ? | ? | – | – | – | Uterus not removed, no dilatation and curettage done. |
| N | 37 | – | + | – | 1 year | + | + | – | + | + | ? | ? | – | – | – | – | Amenorrhea for 6 mon., metrorrhagia 9½ years. |
| N | 40 | + | – | – | None | – | – | – | – | – | 1 mm. | | – | + | – | – | Amenorrhea for 2 mon., menorrhagia last 4 mon. |
| N | 40 | – | – | + | 4 years | + | – | – | – | + | ? | ? | ? | – | – | – | Ascites present. |
| N | 43 | – | + | – | 7 mon. | + | – | + | + | + | ? | ? | + | + | – | – | Metrorrhagia for 1 day. |
| N | 45 | – | + | – | 2 years | + | + | – | – | – | – | + | + | + | – | – | Amenorrhea 2 mon., menorrhagia 22 mon. |
| N | 46 | – | – | + | 1 year | – | + | – | – | + | ? | ? | – | – | – | – | Uterus removed 2 wks. later. Endometrium showed atrophic cystic changes. |
| N | 48 | – | + | – | 2 years | – | + | + | – | + | ? | ? | ? | + | – | – | |
| N | 48 | – | + | – | 1 year+ | + | – | + | + | + | – | + | – | – | – | – | |
| N | 49 | + | – | – | 1 year | – | + | – | – | – | – | + | – | + | – | – | |
| N | 51 | + | – | – | 1 year | – | + | + | – | – | 1 mm. | | – | + | – | – | |
| W | 20 | – | + | – | 2 years | + | – | + | + | + | ? | ? | ? | – | – | – | Uterus not removed. |
| W | 27 | – | + | – | 18 mon. | – | – | + | – | + | ? | ? | – | – | – | – | Intraligamentous granulosa cell tumor. |
| W | 34 | + | – | – | None | – | – | – | – | + | ? | ? | ? | – | – | + | |
| W | 36 | – | – | + | None | – | – | – | – | – | ? | ? | – | – | – | – | |
| W | 37 | + | – | – | None | – | – | – | – | + | – | + | – | + | – | – | |
| W | 40 | – | – | + | 3½ years | – | + | + | – | + | ? | ? | ? | – | – | – | Tumor was ruptured on initial removal contributing to the recurrence. |
| N | 42 | + | – | – | 10 mon. | + | – | – | – | – | – | + | – | + | – | – | Bilateral involvement of ovaries. |
| W | 49 | – | + | – | None | – | – | – | – | – | – | + | – | – | – | – | |

? Status unknown.

Menstrual disorders were noted in seventeen of these cases (Table III). In five cases of granulosa cell tumor, the menstrual disorder was characterized by the presence of amenorrhea followed, at variable intervals of two months to two years, by menorrhagia and/or metrorrhagia. Amenorrhea alone was present in four cases. Two of these were theca cell tumors and two were granulosa cell tumors. In seven cases, three theca and four granulosa cell tumors, either menorrhagia or metrorrhagia or both were noted. No disturbance of the menstrual cycle was apparent in six cases (four theca cell tumors and two granulosa cell tumors, one being malignant).

In the course of physical examination, an abdominal tumor mass was palpated in sixteen cases. These subsequently proved to be ovarian. Of these, five were theca cell and eleven were granulosa cell tumors. The tumors in the remaining seven cases (granulosa two, theca five) were not palpable abdominally.

Associated pelvic pathology was noted in ten of the cases. Nine of the cases were associated with fibromyomas, and the remaining case with fibromyomas and endometrial polyps. In one case of theca cell tumors, Meigs' syndrome was present. The state of the endometrium was satisfactorily described in ten of the cases. Of these, there was mild to marked hyperplasia in eight. In the remaining two cases, the endometrium was 1 mm. in thickness or less. The state of the endometrium was not studied in thirteen cases. In the cases with complete data, there was no correlation of the state of the endometrium and the various disturbances of the menstrual cycle.

Of the five malignant granulosa tumors, none had associated pelvic pathology, two showed no menstrual disorders, and two had amenorrhea. One of the latter may be attributed to a postpuerperal amenorrheic state. A fifth case demonstrated metrorrhagia and menorrhagia.

The case referring to a postpuerperal amenorrheic state was that of a 32-year-old Negro woman, para iii, gravida iii, with a history of amenorrhea of two months following a seven-month pregnancy. The onset of menstruation was at the age of eleven years. There was no history of menstrual disorder prior to her last pregnancy.

On physical examination, there was palpated a cystic mass extending halfway to the umbilicus. The uterus was not enlarged. At operation, the left ovary was found to be transformed into a cystic mass measuring 9.5 by 10.5 by 10.5 cm. The size of the mass suggested its existence for some time during the last pregnancy.

This case is of special interest since Dockerty[2] states that the presence of intrauterine pregnancy with granulosa cell tumor is very rare. Spencer and Hollenback[11] were unable to find in the American literature a case other than the one presented by them of a third trimester pregnancy with a large granulosa cell tumor.

*Feminizing Tumors in the Postclimacteric Period.*—Of the 39 cases reviewed, sixteen (Table IV) had a history of being in the postmenopausal state from three months to twenty-four years at the time of admission to the hospital. Of these cases, nine were granulosa cell tumors, four of which were malignant, and seven were theca cell tumors. In nine of these cases, postmenopausal bleeding was one of the major clinical manifestations which brought them to the hospital for treatment. Five of these latter patients had no associated pelvic pathology, three cases had fibroids, and one woman had a carcinoma of the corpus associated with fibroids and polyps of endometrium.

In the women with no history of postmenopausal bleeding the following associated pelvic pathology was noted (Table IV): fibroids in three cases;

TABLE IV. SUMMARY OF CLINICAL AND PATHOLOGICAL FINDINGS IN FEMINIZING TUMORS OF THE OVARY IN POSTCLIMACTERIC PERIOD

| RACE | AGE (YEARS) | THECA CELL TUMOR | GRANULOSA CELL TUMOR BENIGN | GRANULOSA CELL TUMOR MALIGNANT | AGE OF MENOPAUSE | DURATION OF BLEEDING | INTERVAL OF BLEEDING | DURATION OF FLOW | ENDOMETRIUM ATROPHIC | ENDOMETRIUM HYPERTROPHIC | PALPABLE ADNEXAL MASS | POLYPS | FIBROIDS | CARCINOMA OF CORPUS | MEIGS' SYNDROME | COMMENTS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| W | 52 | - | + | - | 51 | 5½ mon. | 2-3 wks. | ? | - | + | - | - | - | - | - | |
| W | 62 | - | + | - | 44 | 2 years | 14 days | 7 days | ? | ? | + | - | - | - | - | |
| W | 71 | - | + | - | 47 | 3 years | - | Continuous | - | + | + | - | - | - | - | |
| W | 54 | - | - | + | 52 | None | | | ? | ? | + | - | + | - | - | No bleeding since radium insertion. |
| N | 42 | - | - | + | 31 | None | - | - | 1 mm. | | + | - | - | - | - | |
| N | 48 | - | - | + | 42 | 2 years | Irreg. | Irreg. | 1 mm. | | + | - | - | - | - | Recurrent nodules in skin and pelvis. |
| N | 54 | - | + | - | 45 | 8 years | Irreg. | 2-3 wks. | - | + | + | - | - | - | - | |
| N | 53 | - | - | + | 52 | 2 mon. | Irreg. | Spotting | ? | ? | - | - | + | - | - | |
| N | 66 | - | + | - | 53 | No bleeding | | | ? | ? | + | - | + | - | - | |
| W | 50 | + | - | - | 50 | No bleeding | | | ? | ? | + | - | - | - | - | |
| N | 41 | + | - | - | 39 | No bleeding | | | - | + | - | + | + | - | - | |
| N | 64 | + | - | - | 42 | No bleeding | | | - | + | + | - | - | - | - | |
| N | 57 | + | - | - | 50 | 2 mon. | Irreg. | Spotting | - | + | - | - | + | - | - | |
| N | 57 | + | - | - | 50 | No bleeding | | | - | + | + | + | + | - | - | |
| N | 55 | + | - | - | 53 | 1 year | 6-12 wks. | 4-5 days | + | - | - | - | + | - | - | |
| N | 55 | + | - | - | 54 | 2 wks. | - | 2 wks. | - | + | - | + | + | + | - | |

? Status unknown.

endometrial polyps in one case. No associated pathology was noted in three cases. Of the sixteen cases (postmenopausal) there were eight with endometrial hyperplasia, with uterine bleeding in five of these cases and no bleeding in three. Two of the patients that bled had associated pelvic pathology. The endometrium in 3 cases was less than 1 mm. thick. In this group bleeding was present in two cases, and one of the latter had associated pelvic pathology. In view of these findings, it is rather difficult to attribute postmenopausal bleeding to the presence of a feminizing tumor unless one can rule out the presence of associated pelvic pathology such as fibroids, carcinoma of the uterus, and endometrial polyps, which could give rise to postmenopausal bleeding. Endometrial hyperplasia may not have manifested itself clinically because, according to the history, bleeding was absent in three out of eight cases examined, all of which showed endometrial hyperplasia. Nor is postmenopausal bleeding a requisite of feminizing tumors, because this symptom was absent in seven of sixteen cases of feminizing tumors of the ovary appearing in the postmenopausal group. The endometrium was not studied in five cases. In this group, postmenopausal bleeding was noted in two cases, one with associated pelvic pathology. In the remaining three cases, only two had associated pathology.

## Pathological Anatomy

In the study of the pathology of granulosa and theca cell tumors, consideration was given to the gross and microscopic appearance of these tumors, and to associated pathology of the pelvic organs.

*Granulosa Cell Tumors.*—These varied in size from 1½ low power fields to 35 by 20 by 10 cm. The location of the tumor was in the right ovary in nine cases, the left ovary in nine cases, and the right and left broad ligament in one case each. The site in three cases was not given.

Regarding the gross pathological findings, fifteen were cystic, two were solid, and six were not described with respect to the presence or absence of cystic changes.

Microscopically, the granulosa cell tumors studied were subdivided into the following groups: mixed type, 12; cylindromatous, 7; diffuse, 3; and microfolliculoid, 1. In two cases with recurrence of the tumor, the morphologic type varied from the original. In one case of a mixed form (Fig. 1) the recurrence found in the skin at the site of the operative scar four years after the initial operation was of the diffuse type (Fig. 2). In the second case where the original lesion was of the cylindromatous type (Fig. 3), the recurrence, which was removed from the wall of the abdominal cavity two years after the original operation, was of a diffuse type (Fig. 4).

Regarding the endometrium, the histologic status in fifteen cases was unknown. There was hyperplasia in six cases and hypoplasia in two cases (Figs. 7 and 8).

In eighteen of the twenty-three cases studied, information regarding the size of the uterus was obtained either from the description at operation or from observation of the specimen submitted. The standard of comparison was based on normal measurements as given in Gray's Anatomy, namely, 7.5 by 5.0 by 2.5 cm. Diffuse enlargement was noted in seven cases, fibromyomatous enlargement in six cases. Three uteri were of normal size, whereas two were distinctly atrophic. Dockerty[2] and Novak[12] have mentioned likewise an enlargement of the uterus in association with granulosa cell tumor.

Of eight cases of malignant granulosa cell tumor so diagnosed microscopically, we have knowledge of two cases which returned to the hospital for further treatment two and four years later, respectively. In one case, there was recurrence at the site of the surgical incision. The other recurred with multiple peritoneal metastases. The remaining six cases were diagnosed

Fig. 1. Fig. 2.

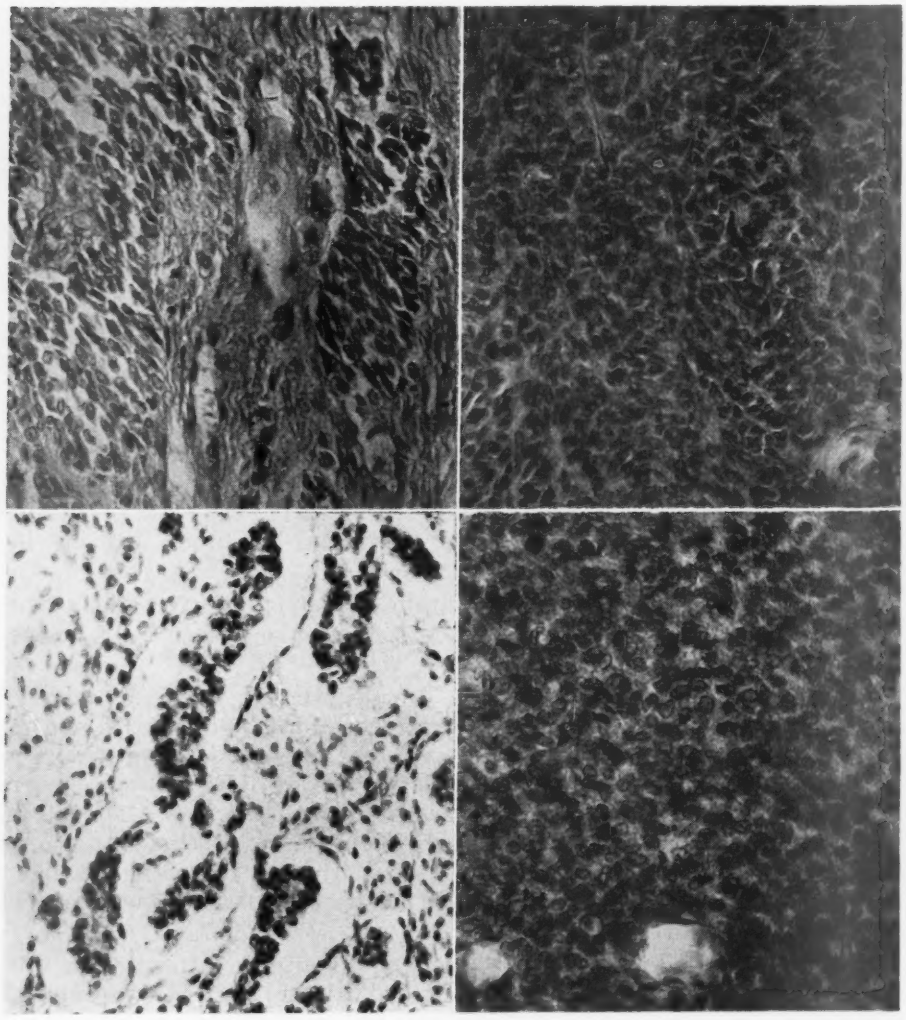

Fig. 3. Fig. 4.

Fig. 1.—Original tumor of ovary. Granulosa cell mixed form. Hematoxylin and eosin stain. Magnification 200×.

Fig. 2.—Showing diffuse recurrent granulosa cell tumor at site of scar removed four years after the initial operation. Compare with Fig. 1, the original tumor. Hematoxylin and eosin stain. Magnification 200×.

Fig. 3.—Showing granulosa cell tumor of ovary, cylindromatous type. Hematoxylin and eosin stain. Magnification 200×.

Fig. 4.—Showing a recurrent diffuse granulosa cell tumor from the abdominal wall two years after the original operation. Compare with Fig. 3, the original tumor. Note mitotic figures. Hematoxylin and eosin stain. Magnification 200×.

malignant on the basis of histologic examination at the time of initial removal of the tumor. According to Novak[12] there are no histologic criteria for the diagnosis of the degree of malignancy of granulosa cell tumors. However, we feel that, in some instances, there is a distinct variation in the size and shape of the nuclei, increased number of mitotic figures (Fig. 5), and invasion of the capsule by the tumor (Fig. 6). These findings may be considered as criteria for the diagnosis of malignant granulosa cell tumor.

Fig. 5. Fig. 6.

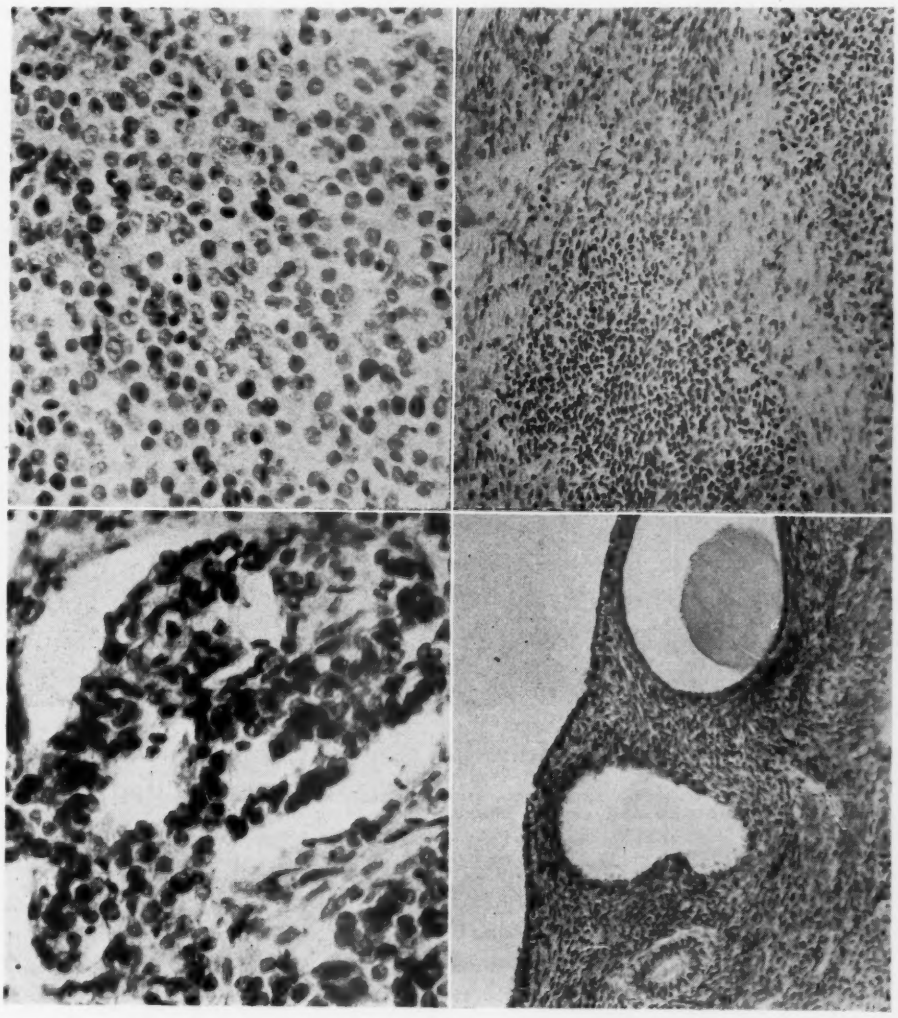

Fig. 7. Fig. 8.

Fig. 5.—Malignant granulosa cell tumor showing mitotic figures. Hematoxylin and eosin stain. Magnification 200×.

Fig. 6.—Malignant granulosa cell tumor, same case as Fig. 5, showing infiltration of the capsule by the tumor tissue. Hematoxylin and eosin stain. Magnification 100×.

Fig. 7.—Showing a trabecular form of a granulosa cell tumor. Hematoxylin and eosin stain. Magnification 200×.

Fig. 8.—Showing atrophic cystic endometrium. Same case as Fig. 7. Hematoxylin and eosin stain. Magnification 100×.

*Theca Cell Tumors.*—As to the location of the sixteen theca cell tumors, eight were found in the right ovary, two in the left ovary, one case was bilateral, and in five, the site was not reported. The tumors varied in size from 8 mm. to 28 by 23 by 10 cm. The tumor mass was usually round to oval in shape with a smooth surface which was at times somewhat lobulated. The section surface was grayish white mottled by large and small bright light yellow areas. All tumors were of a firm consistency, except three of large dimensions, which were partially degenerated and cystic.

The histologic picture presented in these tumors was characteristic and quite uniform in all the cases studied; namely, interlacing bundles of fibrous connective tissue with oval and elongated, small vesicular nuclei. Sudan III stain showed coarse and fine fat droplets diffusely scattered within the cytoplasm of the cell. Regarding the endometrium, the histologic status of sixteen cases was as follows: distinct endometrial hyperplasia in nine cases, atrophic endometrium in four. The status of the endometrium was unknown in three cases.

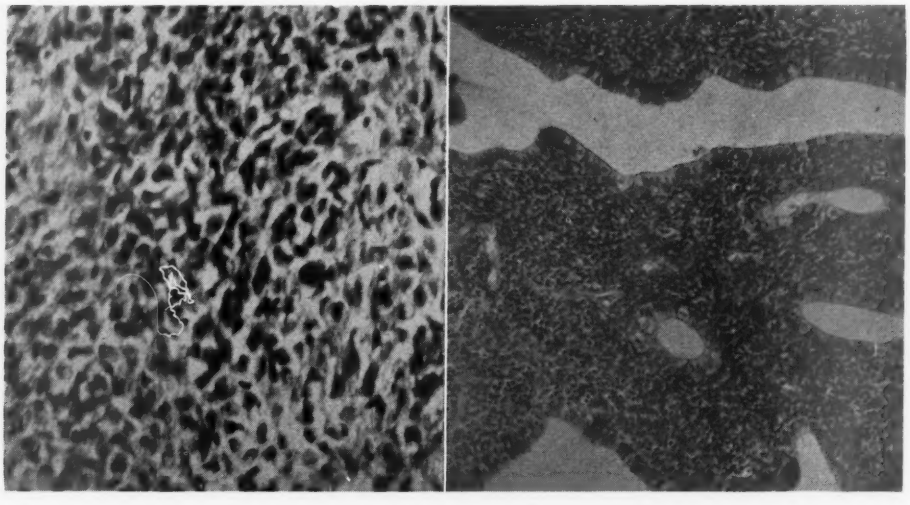

Fig. 9.—Showing an actively proliferating theca cell tumor. Hematoxylin and eosin stain. Magnification 200×.

Fig. 10.—Endometrium in same case as Fig. 9, showing endometrial hyperplasia (Swiss cheese type). Hematoxylin and eosin. Magnification 100×.

One of the cases with hyperplastic endometrium had glandular polyps and a hornifying squamous cell carcinoma in the fundus of the uterus. In a second case with atrophic endometrium, there were several small polyps.

Measurements of the uterus were obtainable in fourteen of the sixteen cases, nine of which were enlarged, due to the presence of fibromyomas, two uteri were normal in size, and one uterus was atrophic. Diffuse enlargement of the uterus was not encountered in our series of theca cell tumor cases. Two uteri measuring less than normal contained small fibromyomas.

The presence of a Meigs' syndrome as characterized by hydrothorax and ascites was noted in one case of a theca cell tuor in a 34-year-old white woman in whom the left ovary was enlarged up to 22 cm. in diameter.

One case of actively proliferating theca cell tumor (Fig. 9) in a 65-year-old Negro woman showed suggestive areas of granulosa cell proliferation. In this case, glandular hyperplasia of the endometrium was present (Fig. 10).

## Summary and Conclusions

The incidence of feminizing tumors in a series of 1,622 tumors of the ovary examined was 3.6 per cent (59 cases). The granulosa cell group comprised 1.78 per cent and the theca cell group, 1.82 per cent.

Thirty-nine cases of feminizing tumor of the ovary were available for detailed study. The incidence was found to be 10 per cent greater than expected in the Negro race, which was due almost entirely to the increased occurrence of theca cell tumor among the Negro.

Of the granulosa cell tumors, 9, or 31 per cent, were malignant, and the greater incidence of these occurred in the older age group, beyond the third decade, indicating conservative surgery before this age.

The incidence of theca cell tumor was found to be 23 per cent greater in the Negro race than expected.

Postmenopausal bleeding is not indicative of feminizing tumor of the ovary, until one has ruled out other pathology. On the other hand, feminizing tumor of the ovary with postmenopausal bleeding may be associated with and obscured by other pelvic pathology.

The absence of postmenopausal bleeding does not rule out the possibility of feminizing tumor of the ovary.

A case of granulosa cell tumor associated with pregnancy in the third trimester has been presented.

Only one case of a carcinoma of the body of the uterus, associated with a feminizing tumor of the ovary (theca cell tumor), was noted in this series.

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## Discussion

DR. EMIL NOVAK, Baltimore, Md.—Dr. Falls has, with his customary thoroughness, given us an excellent review of the clinical characteristics of the feminizing ovarian tumors. These clinical effects are due to the capacity of these tumors to produce estrogen. We can thus understand why in young children these growths bring about the syndrome of precocious puberty; why during reproductive life they produce no secondary sex character changes, but only a disorder, sometimes not impressive, in menstrual amount or rhythm; and why in

postmenopausal women they cause a hypertrophic rejuvenation of the uterus and the appearance of a periodic estrogen-induced type of menstruation.

The clinical feature of these tumors concerning which there is still considerable uncertainty is as to the degree of their clinical malignancy. Everyone is agreed that as a class they are much less malignant than the ordinary forms of primary cancer of the ovary. But some of them are highly malignant, as in a patient in our clinic who, three months after a radical operation, returned with extensive peritoneal carcinomatosis, with later death. Moreover, it should be remembered that recurrences may occur very late, sometimes not for many years, as many as eighten years after operation. I, therefore, feel that many gynecologists and pathologists take these always potentially malignant tumors too lightly.

I have had the opportunity of studying material from something like 165 of these tumors, although of course only a small proportion of these occurred in our own clinic, the majority being sent in from other sources. My impression would be that something like 20 to 25 per cent are clinically malignant. Dr. Falls and his co-workers have evidently used histology as the criterion of malignancy, but this is not always reliable in prognosis. In cases in which recurrence has taken place I have often gone back to the sections of the original tumor and found that they did not differ histologically from tumors which had been clinically benign. On the other hand, when there is marked anaplastic activity, as in Dr. Falls' malignant group, one would expect clinical malignancy as well.

The pathology of these tumors presents many points of interest, but there is not time to discuss this, and I shall comment only very briefly on the matter of histogenesis. There is no longer much doubt as to the inadequacy and incorrectness of Meyer's original concept that granulosal cell tumors arise from rests of redundant granulosa, though this may apply to an occasional case. We must go back to a progranulosal and prothecal stage in ovarian development to explain the origin and the varied histological form of these neoplasms; that is, to the ovarian mesenchyme itself. This is a tissue of tremendous differentiating potency, for from it all types and all degrees of both ovarian and testicular structure can arise.

Two rather recent observations support this view. The first of these is the experimental production of granulosa or lutein tumors by irradiation of the ovaries, as shown by Furth and Furth, Geist and his co-workers, Traut and his associates, and others.

The second recent observation is that tumors of this type develop in intrasplenic or intrapancreatic ovarian grafts in castrated animals, the ostensible factor being the destruction by the liver of the estrogen produced in such grafts, though we still do not know why this factor excites the neoplastic growth.

But both of these recent studies point clearly to an origin of the tumor from the cells of the ovarian mesenchyme or blastema, and a similar histogenesis almost surely applies to human tumors of the feminizing group, and, for that matter, probably also to many masculinizing tumors as well.

DR. E. D. PLASS, Iowa City, Iowa.—This presentation raises the old question of whether the term "feminizing tumor" should be defined in terms of morphology or of function. Dr. Falls and his co-workers are evidently committed to the former since they present little evidence that the tumors they discuss were actually feminizing. On the other hand, some pathologists and clinicians feel that the term is justified only when there is evidence of increased estrogen production.

As a matter of fact, there are valid arguments against either viewpoint. It seems rather futile to talk of a tumor as feminizing when it does not produce sufficient estrogen to provoke endometrial changes or alterations in the secondary sex characters merely because the morphology of the component cells suggests that they should be manufacturing that hormone. And yet, if we accept the designation of "carcinoma" for all of this group of tumors and further accept the postulate that malignant cells generally lose the functional ability of the cells from which they originate, the idea of a strict morphologic classification is not so repugnant. Among Dr. Falls' patients with clinically malignant granulosa-cell tumors, two had no disturbance of menstruation, two had amenorrhea (etiology unknown)

and the fifth complained of menometrorrhagia. These patients were evidently all in the reproductive period of life. By contrast, in the other eighteen patients in this series, there were four with no change in menstruation, seven with amenorrhea alone or with menorrhagia or metrorrhagia, and seven with menorrhagia or metrorrhagia but no amenorrhea. Such small numbers are statistically not significant, but it would appear that those with malignant tumors had more chance for unaffected menstrual cycles, an equal chance of developing amenorrhea, and a considerably reduced chance of having meno- or metrorrhagai which can be presumed to be a reflection of hyperestrinism.

In his sixteen postmenopausal patients, all of whom had nonmalignant growths, seven, or almost half, had no uterine bleeding. Obviously, the hormone production of the latter tumors must have been slight. There is no other evidence to indicate that they were in fact "feminizing."

Restriction of the term "feminizing" to those tumors that produce hyperestrinism would obviously split the morphologic group in two, and demand use of another term. Perhaps it is better to adhere to the term commonly in use to designate these rare tumors that at least arise from cells which normally produce estrin, and to explain the absence of estrin effects to the lack of function imposed by the malignant character of the new growth.

Dr. Falls' finding that both granulosa cell and theca cell tumors are more common in Negro women is interesting but I am not certain that his figures should be accepted at face value. There is no statement concerning the distribution of the 1,622 ovarian tumors between the two races, and such information would seem essential.

It is more than 25 years since I have seen a significant number of Negro patients, but I have a faint memory that they tend to harbor ovarian neoplasms less frequently than do the whites. If this is true, the racial disproportion emphasized by Dr. Falls would be exaggerated. On the other hand, their greater tendency to have uterine fibroids predisposes them to operative intervention and the incidental discovery of ovarian tumors. It would seem worth while to explore further this apparent racial difference and its possible implications on the etiology of this group of tumors.

DR. FALLS (Closing).—As Dr. Novak emphasizes in his discussion that malignancy is difficult to diagnose grossly or microscopically in some of these cases, we agree and emphasize this point in our discussion. I think it is of importance that only one of our malignant granulosa cell tumors occurred in the fourth decade and the rest in later years of life. In handling these tumors, therefore, we feel that one should be conservative in the management of these women in the thirties and twenties, and radical in women 40 and older.

For Dr. Plass' information, there is a ratio of 60 Negro to 40 white patients in the County Hospital, but even allowing for this there still seems to be an increase in the tendency to malignancy among the granulosa cell tumors in the Negro race. We recognize that when you present statistics in per cent when reviewing a group of less than a hundred cases they are of little value, but I feel strongly that it is only by gathering such figures that we can eventually obtain series that are sufficiently large to warrant being considered statistically significant.

# NONNEOPLASTIC OVARIAN CYSTS; THEIR RELATION TO SPIRAL ARTERIES IN THE HUMAN OVARY*†

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THE mechanism of formation of nonneoplastic ovarian cysts in the ovary has long remained in the vague realm of conjecture until recently when, in 1947, an anatomical and physiopathologic cause for their genesis in rabbits was demonstrated.[1]

## Early and Current Concepts of Nonneoplastic Ovarian Cysts

Earlier ideas suggested that chronic infection of the ovary is the etiological factor producing cystic changes in the ovary (Humison 1899, Findley 1904, Smead 1912).[18] Some European workers have mentioned dysfunction of the sympathetic nervous system as a cause of ovarian cysts (Castano and Introzzi 1930, De Coulx and Papoir 1937).[18] Selye[2] states that ovarian follicular cysts are enlarged abnormal persistent Graafian follicles. In discussing the pathogenesis of such cysts he reveals that, according to the currently prevailing view, these cysts develop from fully formed follicles and they give rise to a functional disturbance either because the follicle persists for an unusually long period or because there is a continuous pressure of repeated follicle formation without luteinization (Miller, Schröder).[2]

While the development of cysts from follicles is well established, the physiological mechanism which elicits them is still not fully understood. It is generally believed that "they are caused by a hormonal dysfunction, more specifically by a derangement of the normal sequence in the elaboration of follicle stimulating and luteinizing gonadotrophic hormones."[2] This belief, it is said, is supported by the fact that metropathia hemorrhagica most frequently occurs at the beginning and end of normal menstrual life, and those individuals who are especially predisposed are women who have gone through a large number of pregnancies. Selye observes that the view that follicle cysts result from inflammatory conditions causing a connective tissue mechanical barrier around the follicle and preventing its rupture, has now been abandoned. Nevertheless, he asserts that this mechanism may yet come into play in the development of small cystic degenerative changes in the ovary (Tietze).[2] The etiology of corpus luteum cysts is likewise not completely understood.[2]

Taylor[3] in 1936 supported a hormonal causation for the etiology of ovarian cysts. He noted that anterior pituitary hormone injections in laboratory animals and human beings may result in the development of an increased number of follicles, some of which assumed cystic proportions. He brought out the fact that cystic ovaries are noted to be present with chromophilic adenoma of the pituitary, with various other intracranial lesions, as well as

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hydatidiform moles and chorionepithelioma. Polycystic ovaries found in the newborn were also stated to be due to a hormonal influence.

## Structural Components of Nonneoplastic Ovarian Cysts

The structural components of cysts merit consideration. Geist[4] mentions that in all probability the fluid content of the follicle cyst is a transudate though some of the fluid is produced by granulosa cells since it contains estrogens. When the follicle becomes many layered, the liquor folliculi which accumulates consists of a combination of transudate from the vessels, products of cell degeneration and possibly cell secretion. He further states that atretic follicles are caused by a regression of unruptured follicles. The cystic form is common in atresia of large follicles. Sometimes, however, due to many repetitions of the atretic process, multiple small cysts may almost replace the normal tissues of the ovary. The result of this is the typical microcystic or polycystic ovary so frequently encountered in pelvic surgery. The increase in size of a cyst is not due to cellular growth but to an increase in fluid. Geist[4] differentiates persistent follicles, hydrops folliculi (the term used for small persistent follicle and follicular cysts) and microcystic ovaries on a quantitative rather than a qualitative basis. In the early stages of development of the cystic follicle, the fluid is supposed to be produced by cell secretion and is later augmented by transudation. Estrogens were demonstrated in this fluid by Moulonguet and Frank[4] and by Watts and Adair.[19] Increased follicular tension appears gradually to destroy the ovum and flatten the epithelium which finally disappears. Regression of a cyst may occur by resorption of fluid, according to Geist.[4]

This author states also that lutein cell cysts develop either from retention of fluid in atretic follicles augmented by a transudation of fluid or from liquefaction of a corpus luteum with subsequent transudation. The quantity of fluid secreted by the epithelial lining is considered to be minimal.

Novak[5] mentions that the liquid in atretic cystic follicles contains little or no estrogen. Under certain conditions, large cystic follicles in which the ovum and granulosa are not degenerated show a rich estrogenic content.

## Ovarian Spiral Arteries, Anatomical Patterns and Physiopathologic Relationships

In 1947 Reynolds,[6] working with rabbits, rediscovered spiral arteries in the ovary. He demonstrated that one of the functions of spiral arteries was adaptation to growth of the ovary when this structure is stimulated by gonadotrophins.[1] This process is dynamic in a progressive and regressive fashion, since the coils become extended during the period of ovarian enlargement and become recoiled as the growth response subsides. He also suggested that a helix of gradual diminishing diameter which comprises the form of the ovarian spiral artery offered a mechanism whereby the blood pressure from the main ovarian artery could be reduced to osmotic pressure requirements within the limited confines of the ovary and equalized blood pressure throughout the ovary.[6] Reynolds induced the formation of corpus hemorrhagicum cysts in rabbits by the injection of gonadotrophins.[1] He found that in contradistinction to the equal and orderly "paid out" coils of the spiral arteries found to be associated with normal ovulation and luteinization, a distortion of localized portions of the spiral artery occurred in the neighborhood of corpus hemorrhagicum cysts.

Normally, the architecture of a spiral artery in the ovary lends itself to constant and gradual lowering of blood pressure along the length of this vessel. In an area of localized distortion of a spiral artery this gradual lowering of blood pressure is lacking. There is transmitted to the capillaries it supplies a greater blood pressure than would normally occur, had spiraling been present. More simply, the hydraulic principle of axial streamline flow replaces to a greater or lesser extent the pressure-reducing mechanism of flow in a curved system in which the axial stream is deflected to the outer curvature of the coil. Since the blood pressure in the straightened segment is greater than normal, an excess passage of fluid (transudate) will take place from the derivative capillaries to the follicle or corpus hemorrhagicum located in the neighboring area, since these are the only structures present in the compact ovarian stroma that can accommodate excess fluid. These observations fit in beautifully with the previously mentioned concepts of other workers, that most of the fluid in nonneoplastic cystic ovaries consists of a transudate and it offers for the first time a physiological basis to account for them. These observations were made in rabbit ovaries.

Following in the footsteps of the above work and using an almost similar technique, plastic casts were made of the vascular tree in human ovaries.[9] A later publication described the vascular patterns (arterial and venous) in the human ovary.[10] Just as in the rabbits, although the vascular architecture is much more complex, the numerous arterial branches of the human ovarian artery were found to be in the form of a helix of gradual diminishing diameter, running counterclockwise.

In normal adult ovaries the main ovarian artery at the hilar area was found to be undulant and tortuous. In one instance a well-formed spiral was observed. Primary, secondary, and tertiary branches were noted proceeding from the main ovarian artery to the periphery in a parallel fashion. The primary branches arising from the main ovarian artery in the hilus were undulant, tortuous, often flattened, and only occasionally spiraled. Secondary branches coming off the primary trunks were smaller in diameter and showed a greater measure of spiraling. The tertiary branches arising from the secondary branches were smallest in diameter and showed the greatest degree of spiraling. The tertiary branches were the smallest arterial vessels demonstrated. The latter gave rise to the terminal arterioles which supply the ovarian stroma.

It was also found that growth and development of arterial ovarian branches must be added to the known trophic activities of estrogens. Sparse, small, thin, and widely spaced ovarian arterial branches with only slight spiraling were found to be related to the menopause.[10, 12] Hypertension and the presence of grossly sclerotic ovaries showed no relation to the degree of profusion and spiraling of arterial vasculature.[10, 12] Maternal hormones influenced the growth, development, and spiraling of late fetal and early infant ovarian arterial branching.[10, 12]

## Technique

The method used was as follows: Postmortem and surgical specimens were utilized. A suitable-sized needle, usually 18 gauge, was inserted into the uterine or ovarian artery or vein. In the infant and fetus, the lower aorta was injected. The vessel was tied tightly around the needle with a ligature. The free stump (either uterine or ovarian) was clamped. A small amount of acetone was injected into the needle and the needle cup was filled with the same material. This was a precaution taken to prevent premature hardening of the plastic. Then vinylacetate in acetone was rapidly injected. The injected specimen was then incubated in a corrosion bath. Equally good casts

were obtained no matter what route was used due to the free inosculation that exists between the uterine and ovarian vessels. Red vinylite was used for arteries and blue for veins. Cysts and corpora lutea were injected locally within their respective walls. This proved to be a more accurate method for localizing the cysts in relation to the distorted vessels than were pictures or drawings of gross cysts or corpora lutea on the fresh ovary, as originally attempted early in this work. This study was concerned with follicular and corpus luteum cysts. Thus far more than sixty sets of human ovarian casts have been prepared and carefully studied.

Since we were dealing with human subjects no sequent continuity could be attained with respect to cyst formation, as was the case with the study on rabbit ovaries, where tissues were taken at spaced intervals following injection of the gonadotrophins.[1] The ovarian vasculature in the rabbit, so much simpler than that of the human being, might be thought of as a simple unit which, when multiplied many times, forms the picture of the complex human ovarian vessels. It is interesting to note the parallel changes occurring in the two species in the presence of cysts, in one in association with a simple vasculature, in the other in association with a complex one.

## Results

**I. Adult Ovarian Cysts.—**

*A. Spontaneous.—*

Ovarian cysts were observed to form a solid cast following direct injection with the vinylacetate followed by corrosion (see Fig. 1). However, a corpus luteum due to its profuse vascularity has the appearance of a coarse loosely woven basket (see Fig. 2). Compare with casts of rabbit corpora lutea.[6] Fig. 3 is a specimen that shows characteristics of a cyst within a corpus luteum as depicted by the gross cast configuration. More will be mentioned about this specimen later. The solid-looking cysts often may be seen nesting in a fringe or a beard-like network of fine vessels that appear to be venous in configuration as do the basket-like vessels in the corpus luteum. However, those vessels in the vicinity of the cyst are much finer. (Compare Fig. 1 with Fig. 2.)

As originally discovered and described in rabbits,[1, 7] ovarian structures such as cysts or corpora lutea will cause a "paying-out" or uncoiling with some degree of flattening of the arteries in the neighboring region. These are especially noted in the tertiary branches. This "paying-out" of spirals will occur in an intra- and inter-loop form. (See Figs. 1, 2, 3, and 4.) Compare these with rabbit specimens.[6, 7] It is interesting to note that cysts or corpora lutea located peripherally often seem to have pointing to them one or a few isolated arteries (tertiary branches) with a varying degree of "paying-out" or uncoiling. These vessels appear to stand out as a sentinel from the rest of the arterial tree. (See Figs. 1, 2, and 3.)

The above described process of arterial distortion in relation to a corpus luteum or a follicle will undergo restitution during the regressive phase of its progress.[7] A cyst, however, may not show such dynamics. As originally suggested by Reynolds,[1] the segment of straightened spiral will transmit a greater blood pressure locally and will thus encourage cystic growth. Greater segmental blood pressure can cause an increased flow of fluid from capillaries to neighboring tissue. In such a manner a small follicle or a corpus luteum increases rapidly in size. If this extends a coil, there results an increased blood pressure in an originally spiraled segment and thus it becomes the initiating mechanism whereby it may itself become an irreversible cystic growth.

Fig. 3 is from a specimen showing the basket weave of a corpus luteum containing within it the solid cast of a cyst. At the pointed end of this inner

Fig. 1.—Cast of ovarian arterial and venous pattern, from a 46-year-old woman, para i, gravida i, with history of fibroid uterus and metrorrhagia.

*Note:* Follicle cyst appearing as a solid cast with a fine vascular fringe around it. The arterial and venous configuration are quite different. There is "paying-out" or uncoiling of arterial spirals in the vicinity of the cyst. Arteries leading to the cyst are few and stand out, in "sentinel" fashion. The fine vascular fringe around the solid cyst is venous in configuration. Compare with Figs. 2 and 4. Observe how with the intermingling of the arteries and veins, venous engorgement might affect uncoiling of the arteries. (×1½)

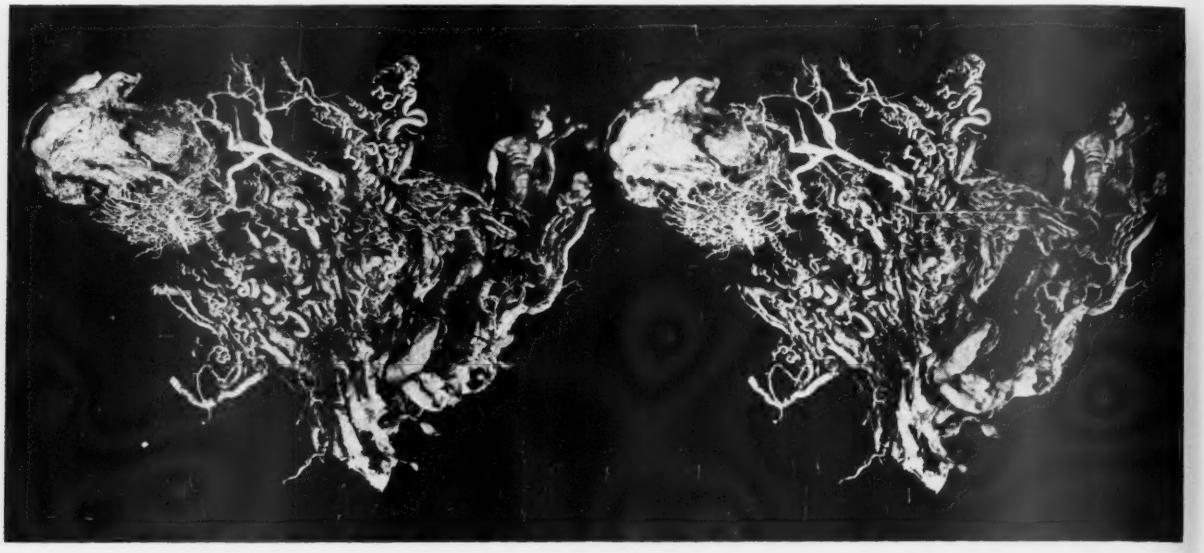


Fig. 2.—Cast of ovarian arterial pattern from a 35-year-old para ii, gravida iii, with history of fibroid uterus and metrorrhagia. Note the coarse basketlike weave of the cast of a corpus luteum to the right. The smaller solid body to the left is a cyst surrounded by a fringe of fine veins. Compare with Fig. 1. Note "sentinel" arteries and degree of "paying-out." Compare size of corpus luteum and degree of "paying-out" of vessels with Figures 1, 3, and 4. (×1½)

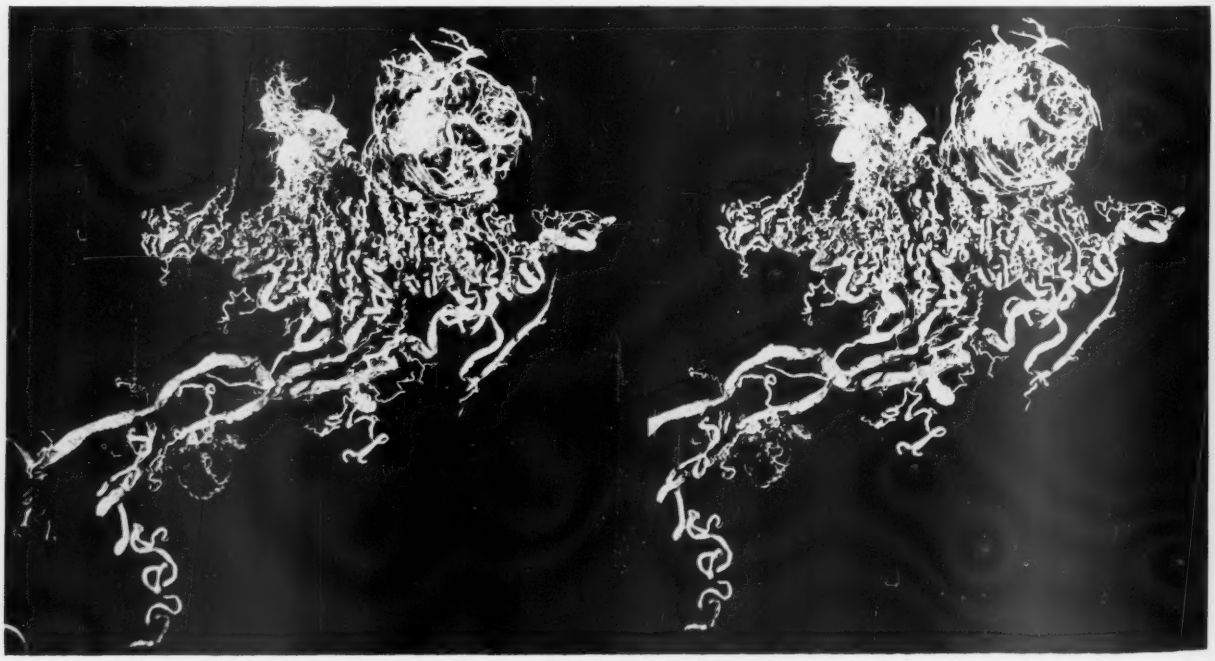


Fig. 3.—Cast of ovarian arterial and venous system from a 35-year-old para 0 gravida 1, with history of fibroid uterus and menometrorrhagia. Note that structure in upper left area presents cast characteristics of a solid cyst and the coarse basketlike weave of a corpus luteum. Note uncoiling of arteries, particularly the extremely "paid-out" "sentinel" vessel near the lower left corner of the structure. Microscopic study of the tissue of this structure reveals an early lutein cyst (Fig. 5). Compare the size of the structure and the degree of uncoiling with Figs. 1, 2, and 4. The solid body to the right of the cast is an artefact due to plastic leakage from a ruptured vessel. (×2)

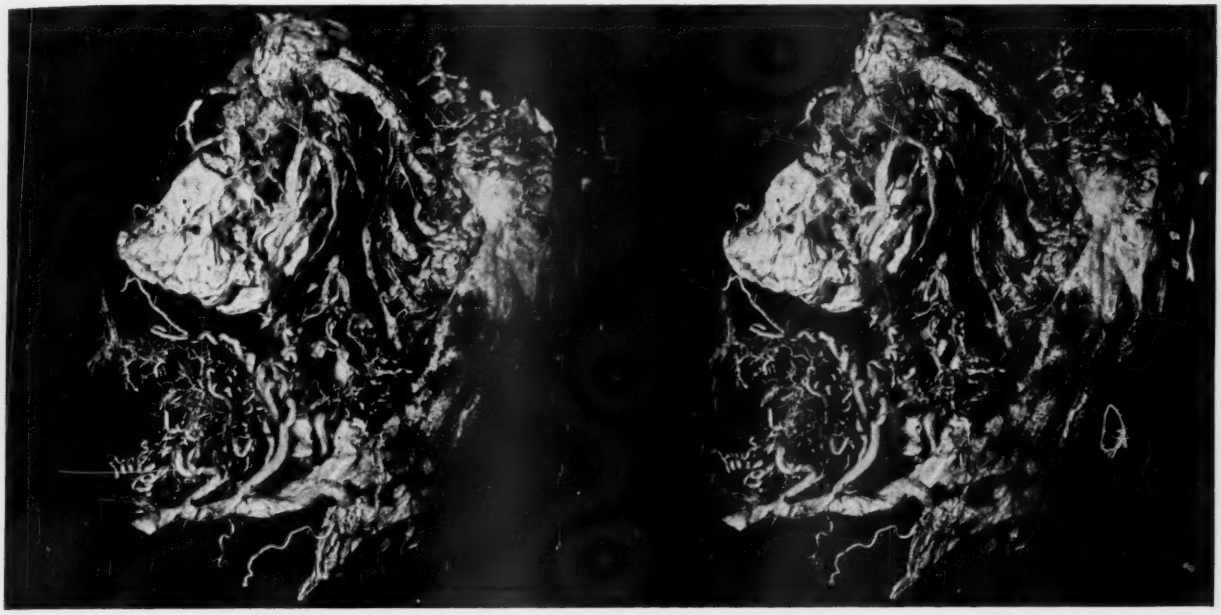
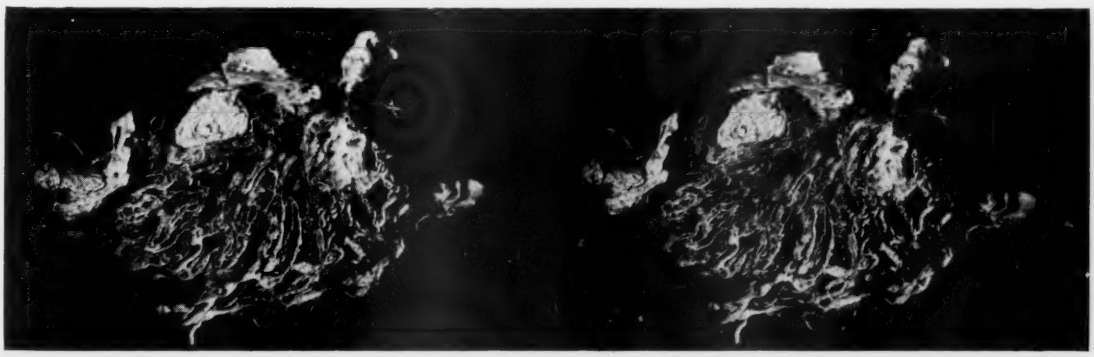


Fig. 4.—Cast of ovarian arterial and venous pattern of a 41-year-old nullipara with a fibroid uterus. The ovaries contained multiple cysts. The solid casts of five cysts are visualized. Note the uncoiling of spiral arteries in the vicinity of cysts. Compare size of structure (cyst) and degree of uncoiling of arteries with those in Figs. 1 and 2. Note the differential characteristics of arteries and veins and observe how venous engorgement could affect the arterial coiling as in Figs. 1 and 3. (×1½)



cystic cast can be clearly seen an extremely "paid-out" artery. Compare with segmental "paying-out" in rabbits.[1] A large part of its distal portion is practically straightened. The marked character of its distortion is most striking after comparison with other specimens. This vessel seems to be beyond the stage of any possible restitution to its original spiraled form.

In other words, here we have a specimen that shows evidence of both a cyst and a corpus luteum according to the cast configuration. Careful histological examination of the tissue of this structure reveals in an interesting manner a lutein cyst practically in the genesis of formation as evidenced by the presence of a slight amount of fibrous connective tissue (see Fig. 5). Presented by this cast then is remarkable evidence of a corpus luteum in process of its development into a lutein cyst adjacent to an extremely "paid-out" spiral artery.

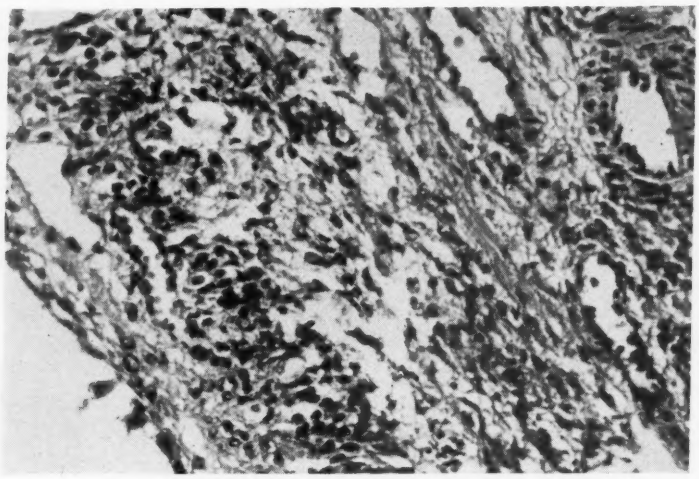


Fig. 5.—Microphotograph showing section of early lutein cyst. This tissue was taken from the ovarian structure shown in Fig. 3. Note the slight amount of fibrous connective tissue near the cyst lining. (×360)

In a comparative study of casts (see Figs. 4, 1, 2, and 3) a proportional relationship can be observed between the size of the ovarian structure (cyst or corpus luteum) and the degree of arterial "paying-out." Fig. 4 shows comparatively smaller cysts. Compare this with Figs. 1 and 2, which have larger cystic structures and a corresponding degree of increase in the "paying-out" of arteries. Fig. 3, although it is pictured at a magnification of ×2, whereas the former casts are ×1½, has obviously a larger ovarian structure and clearly has greater arterial distortion.

*B. Postoperative.*—

Venous casts are morphologically quite different from those depicting the arterial system. The veins are in the form of a pampiniform plexus at the hilar area. They are large, irregularly tortuous, markedly flattened, and often appear matted. (Compare Fig. 6 with Fig. 4. See Figs. 1, and 2 and note that vessels of cyst and corpus luteum are venous in nature.) The venous vasculature is usually most dense at the hilar area. The various branches anastomose with each other very readily. At the distal portion they end in small straight veins that are never spiraled. Occasionally small pouchlike protuberances are noted in larger branches in the vicinity of the hilus. Sometimes a beading may be noted in the medium veins that may be mistaken for spiraling on superficial examination.

Figs. 3, 1, and 4 are casts in which both the arterial and venous systems in the ovaries were injected. The arteries were injected with red vinylite

and the veins with blue. These are not as distinguishable by hue in black and white photography as they are by configuration. Since the venous plexus is usually most dense at the hilar area, this might explain the fact that the primary arterial branches show few spirals. It is conceivable that distortion of the spiral arteries can depend on the degree of engorgement found in the ovarian veins. (See Fig. 7.)

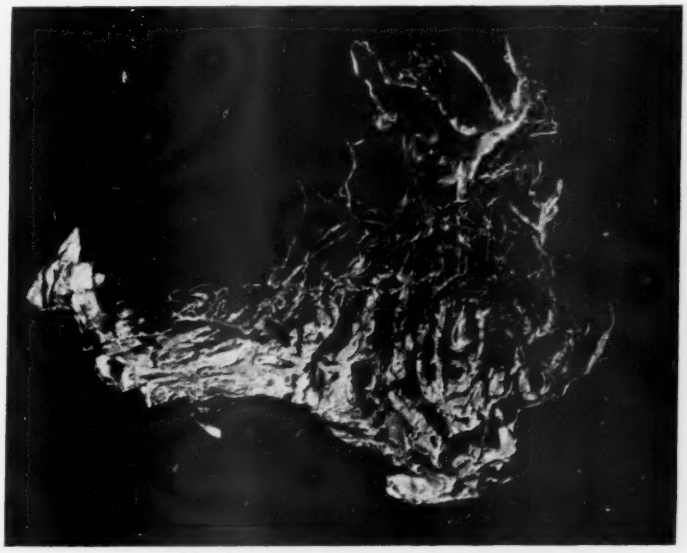


Fig. 6.—Cast of ovarian venous pattern from a 39-year-old para iv, gravida viii, with past history of menometrorrhagia. Note pampiniform plexus, matting, irregularity, flattening, anastomoses, and absence of spiraling. Compare with arterial casts. (×2)

It is of interest to note the large vein or veins that may be found in the mesosalpinx (Fig. 7). Upon them fall the burden of venous drainage from all the surrounding areas, including the tube and ovary. Veins in the infundibulopelvic ligaments and ovarian ligaments are smaller. Experienced gynecologists have long been aware of the fact that the formation of postoperative cystic ovaries were not infrequent following certain pelvic operations. Taylor[3] in 1936 discussed postoperative ovarian cysts following hysterectomy, salpingectomy, and oophorectomy for cystic conditions. Following hysterectomy, he states that one cause might be a compromised blood supply but mentions that the remaining blood supply from the infundibulopelvic ligament makes this idea improbable. A second theory would explain these postoperative ovarian cysts on the basis that the endometrium of the removed uterus is an endocrine organ and its presence is necessary for the preservation of normal ovarian function. However, he believed that a more probable explanation would be that the ovary at the time of operation was already cystic and that the manifestation of postoperative cystic ovaries is dependent on a continuation of some preoperative process.

The responsible causation of postoperative cystic ovaries following salpingectomy is laid to "questionable" factors such as the operation, associated inflammatory disease, or a continuation of preoperative changes. Recurrent cystic ovary following the removal of the other ovary for cysts is explained by the fact that the original condition had bilateral tendencies.

Weed and Collins[18] observed in young females large prolapsed multicystic ovaries with an associated congestion in the veins of the infundibulopelvic and broad ligaments. This suggested to them that altered position and vascularity was the underlying cause of the cystic condition. Utilizing rabbits and dogs as experimental animals, they found that artificial prolapse of ovaries in these animals produced chiefly vascular changes, causing follicular cysts and an increased thickness of the tunica albuginea.

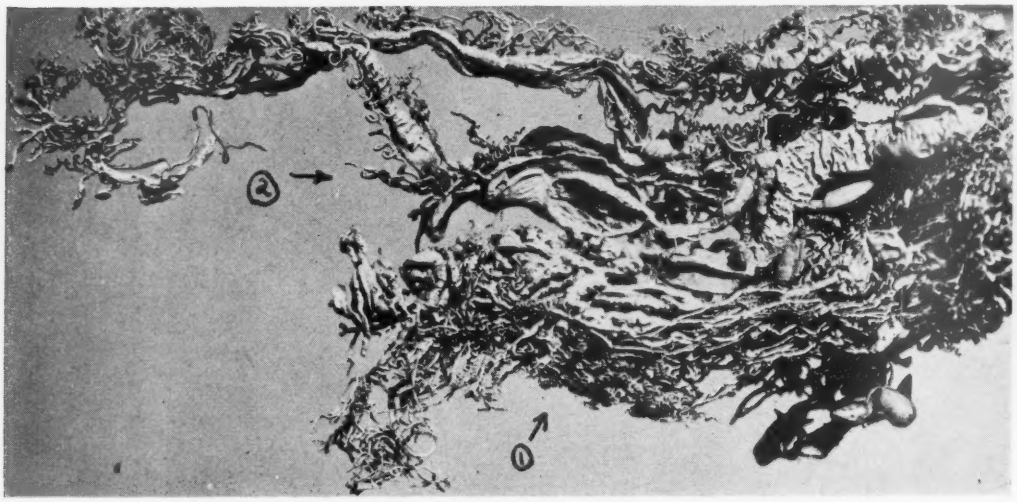



Fig. 7.—Cast of left ovary, mesosalpinx, tube, and part of uterus. Posterior view. (1 points to ovary, 2 to mesosalpinx.) Patient was a 46-year-old nullipara with a fibroid uterus. The veins are lighter in hue than the arteries. Note how intimately close the veins and arteries lie. In the vicinity of the pampiniform plexus at the ovarian hilar area some uncoiled primary arterial branches can be noted. The effect of a venous engorgement on arterial spiraling can be clearly visualized. Note the large veins in the area of the mesosalpinx. These drain the tube and ovary. Two good-sized veins can be seen leaving the ovarian pampiniform plexus and entering the large venous channels in the area of the mesosalpinx. In comparison, observe the small caliber veins in the infundibulopelvic and ovarian ligaments. Due to fixation and folding at the mesosalpinx, the veins in the mesosalphinx appear to lie closer to the ovarian area than they actually should.

TeLinde[11] mentions postoperative ovarian cysts following a salpingectomy. He states that these cysts are prone to develop if the clamping instrument does not hug the base of the tube closely.

It is conceivable that clamping and cutting the large prominent vein or veins in the mesosalpinx will cause the veins in the ovary to become engorged due to the fact that the returning blood has fewer channels of egress than before. The veins of the infundibulopelvic ligament and the ovarian ligament are of the smaller caliber. Such engorged veins in the ovary can then institute a "paying-out" process in the ovarian arterial branches with a resultant cyst formation as described above, provided there are suitable ovarian structures (follicles or corpora lutea) in the vicinity.

Following a hysterectomy venous egress is blocked via the large vein or veins in the mesosalpinx, and via the small veins in the ovarian ligament. The load of venous return is then thrown on the smaller veins in the infundibulopelvic ligament. Here, too, an engorgement of ovarian veins can take place with a resultant distortion of spiral arteries.

**II. Infant Ovarian Cysts.—**

Cystic ovaries in the newborn and infants have been known to exist for a long time (Roikitansky 1861, DeSinety 1878, Von Franque 1898, Runge

1906, Benthin 1910, and Delestre 1911).[13] Runge in a study of fifty cases found them in the newborn and in children up to the age of 9 years. He is reported as stating that they occurred with greater frequency in infancy and childhood as compared with intrauterine life.[13]

Fig. 8.—Cast of ovarian artery from a seven-month premature infant who lived for only a short time post partum. Only slight spiraling can be observed in the small branches. Compare with Fig. 9. See Table I. (×5)

Spivak, in 1934, found fourteen follicular cysts among thirty-six infant cases studied.[13] These comprised 39 per cent of the whole group. The cysts on the average were 5 to 6 mm. in diameter, but ranged from 1 mm. to 1.5 cm. In all cases, cysts were found in infants over 3 weeks of age.

Out of the whole group of associated uteri studied, there were only five with distinct and pronounced hypertrophy of the glandular elements. Cystic ovaries were found in only two out of this group of five uteri.

Spivak believed that cystic follicles in the newborn are due to anterior pituitary hormone, based on the work of Engle and Smith,[14] and although Runge and Benthin found cystic ovaries in all ages up to 9 years of age, she did not believe that cysts were long lived, since Engle and Smith showed cysts induced in mature animals with anterior pituitary hormones were short lived.

A series of seven fetal and infant casts were prepared as previously described[9, 10] (see Figs. 8 and 9). The data on these specimens are striking when tabulated in a chronological fashion in Table I.

TABLE I. OVARIAN ARTERIAL BRANCHES IN PREMATURE AND INFANT OVARIES

| NO. | AGE | GROSS OVARIES | ARTERIAL CONFIGURATION |
|---|---|---|---|
| 62 | Premature—6 months | Normal | No spiraling, few branches |
| 31 | Premature—7 months | Normal | Slight spiraling |
| 44 | Full term, stillborn | Normal | Slight spiraling |
| 36 | Full term, 7 hours | Normal | Slight spiraling |
| 47 | Full term, 9 days | Normal | Excellent spiraling and more profuse branching |
| 43 | Full term, 3 months | Two small atretic follicular cysts, left ovary | No spiraling |
| 59 | Full term, 4½ months | Polycystic | Some spiraling with evidence of "paying-out" and many straightened arterial branches |

It is interesting to note that slight spiraling is observed to exist from late in fetal life until shortly after birth. Nine days post partum, excellent spiraling and more profuse branching were present. At 3 months of age, there is no arterial spiraling present but two small atretic follicular cysts were noted in the left ovary. The 4½-month full-term infant had bilateral polycystic ovaries. The arterial ovarian cast showed some spiraling with evidence of "paying-out" and many straightened arterial branches.

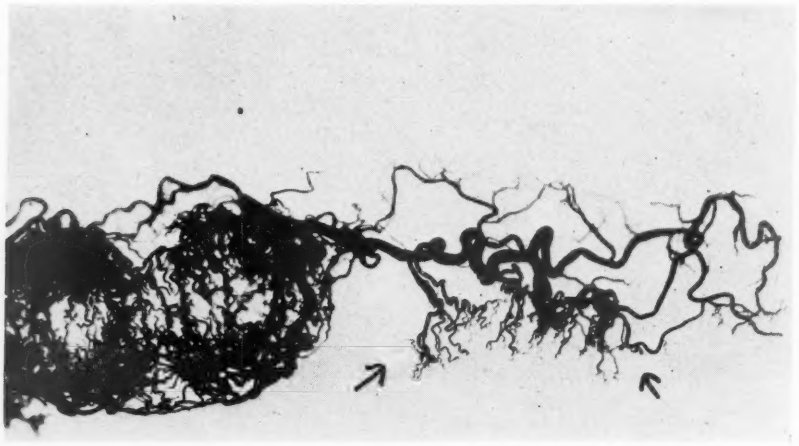


Fig. 9.—Cast of ovarian artery from a full-term infant who expired nine days post partum. (Arrows point to ovarian vasculature.) Note excellent spiraling in smaller branches and profuse branching. See Table. I. Compare with Fig. 8. Denser object to the left of ovarian vasculature is a cast of uterine arteries.

In summation then, growth and development of ovarian arterial branching and evidence of arterial branch spiraling is noticeable late in fetal life and reaches its greatest development approximately one week after birth. From the evidence at hand, regression occurs over a period of months. These observations follow closely other well-known genital phenomena in infants, such as vaginal hypertrophy, breast engorgement, lactation, and endometrial bleeding,[15] which are believed to be caused by a maternal hormonal influence. Complete infantile vaginal atrophy will appear after the first three weeks of postnatal life and seventy-five per cent of infants will lactate until three to four months of age.

Scammon[16, 17] in his studies on fetal and neonatal uteri, suggested that late in fetal life a secondary growth increment supplemented the normal growth rate of the uterus. The secondary growth increment, he stated, presumably was due to a stimulation produced by a hormone either placental or ovarian in origin. This secondary increment is lost after birth.

From all of the above evidence, it has been suggested that growth, development, and spiraling in fetal and infant ovarian arterial branches is dependent on a maternal hormonal influence.[10, 12]

It is important to note that in this series cysts in the infant ovaries appear at a time when spiraling in the arterial branches is disappearing or is completely gone, about the third to fourth month of age (see Table I). Spivak,[13] as mentioned earlier, found that most infant ovarian cysts occurred after three weeks of extrauterine life.

Geist[4] states that after the sixth month of intrauterine life the primordial follicle is capable of developing into a Graafian follicle and that despite the fact that follicles are continuously degenerating, the number of Graafian follicles increases. In the full-term fetus, the ovary presents follicles in all stages of maturation from primordial to ripe Graafian follicles. He also mentions a corpus luteum in a fetal ovary discovered by Runge.

It would seem, then, that a process similar to that which occurs in cystic development in rabbits[1] and in adult human beings may occur also in infant ovaries. That is, developing Graafian follicles or corpora lutea (rare) can cause a "paying-out" or an uncoiling of a spiral artery. This will cause an increase in blood pressure in a straightened segment which is in the vicinity of the structure that caused the uncoiling. There will, therefore, be an increased passage of fluid from the capillaries arising from the uncoiled arterial blood vessel. This transudate will then be accommodated by the follicle or corpus luteum since the rest of the ovarian tissue is quite dense.

Following parturition, withdrawal of the maternal hormonal influence may cause a gradual loss of spiral formation in the ovarian arterial branches over an extended period of time. The loss of spiraling or uncoiling with the resultant presence of straightened arterial branches will then favor cyst formation as previously described, provided the necessary ovarian structures (follicles, corpora lutea) are in the neighboring locale. This concept can explain why the greater percentage of infant cystic ovaries occur after three weeks of extrauterine life.

## Summary

Ovarian cysts were noted to give a solid cast following direct injection of the blood vessels with vinylacetate plastic. The corpus luteum, due to its profuse vascularity, will form a cast with the appearance of a coarsely woven basket.

Evidence was presented of the association of cyst formation and localized distortion of spiral ovarian arteries, confirming the work in rabbits.

A cast showing characteristics of both the cyst and the corpus luteum with histological evidence of an early lutein cyst was presented.

A comparative study of cystic and corypus luteum casts showed a proportional relationship between the size of the ovarian structure (cyst or corpus luteum) and the degree of ovarian arterial spiral distortion.

The suggestion was made that ovarian venous engorgement following embarrassment of venous drainage due to certain gynecological operations can be a causative factor in the formation of ovarian cysts.

Evidence that growth, development, and arterial spiral formation in fetal and infant ovaries are dependent on maternal hormones was presented and discussed. It is believed that infant ovarian cysts follow a similar process as in adults, i.e., a localized distortion of ovarian spiral arteries. In addition, withdrawal of maternal hormones post partum, causing a loss of spiraling may enhance this process and explain the increased presence of infant cystic ovaries after three weeks of extrauterine life.

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# THE EARLY DIAGNOSIS OF CARCINOMA OF THE CERVIX WITH EMPHASIS ON ROUTINE BIOPSY*

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THE chance for recovery from cancer is inversely related to the extent of the disease when treatment is instituted; therefore, the early diagnosis of cancer is mandatory if good results are to be obtained. The addition of the Hinselmann colposcope and the Schiller test to our clinical armamentarium stimulated gynecologists in their efforts toward early recognition of cervical cancer; subsequent studies, however, have shown these methods to be of limited value. In 1943, Papanicolaou and Traut introduced the use of vaginal smears in the diagnosis of uterine cancer. The validity of this method has been confirmed by Meigs,[1] Ayre,[2] Warren and Gates,[3] and many others. However, its usefulness is limited by the paucity of expert cytologists. This test will not be widely available for many years. Furthermore, it is generally agreed that a diagnosis made by a vaginal smear must be confirmed by histologic examination. Biopsy still remains the one decisive diagnostic procedure by which early cervical cancer can be recognized. Although the controversy concerning preinvasive carcinoma[4] still continues, the criteria for the histologic changes in the cervix required to justify a diagnosis of early invasive carcinoma have been well established by TeLinde and Galvin,[5] Novak,[6] Meyer,[7] and others.

Very early carcinoma of the cervix usually produces no symptoms. Phaneuf,[8] Cox, Buhler and Mixson,[9] Novak,[10] and TeLinde and Galvin[5] have pointed out that early carcinoma is clinically indistinguishable from benign cervicitis. All clinics follow the policy of performing a biopsy whenever a questionable or suspicious lesion of the cervix is discovered. Although routine biopsy of the cervix is employed in some clinics,[11] reports on the result of this practice are few. Phaneuf[8] discovered ten cervical carcinomas in one hundred consecutive biopsies. Cox, Buhler, and Mixson[9] found two invasive carcinomas and three intraepithelial lesions in one hundred ten routine biopsies. The incidence of carcinoma in other studies of apparently benign cervices is significant, Schiller,[12] reporting 1.41 per cent, TeLinde and Galvin[5] 1.3 per cent, Pund and Auerbach[13] 3.9 per cent (preinvasive).

## Materials and Methods

The clinical and pathologic records of the obstetric and gynecologic outpatient department of the North Carolina Baptist Hospital have been re-

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viewed for the five-year period from July 1, 1943, to July 1, 1948. Ten thousand fourteen visits have been made to the department during this period. All of the patients were of the white race. The vast majority of them were referred for examination by their family physician or from one of the collateral divisions of the clinic.

Each pelvic examination in our clinic includes careful inspection of the cervix through a Graves speculum with bright light. Each patient is examined by a senior medical student and the resident physician, or a member of the attending staff. A biopsy specimen is taken from the cervix whenever a deviation from a completely normal appearance is found. During the five-year period 1,797 cervical biopsies have been made—an incidence of 17.8 per cent of the patient visits to the clinic.

Cervical biopsy specimens are taken in the outpatient clinics without anesthesia. Cauterization of the wound is used to control bleeding when necessary, but in the majority of cases insertion of a vaginal tampon is sufficient. No significant complications have occurred in the present series of patients. Biopsy of the cervix is also a routine procedure when dilatation and curettage are performed in the hospital, regardless of the clinical appearance of the cervix.

Tissue is taken by the punch biopsy instrument, the electrosurgical loop, or a scalpel, depending upon the choice of the examiner. Several pieces of tissue are usually taken in each case. Often, when a small cervical lesion is present, all of the diseased tissue is removed and submitted for pathologic examination. It is recognized that cancer has a predilection for the tissue at the external os and the junction of the squamous and columnar epithelium. This tissue is invariably included in the biopsy specimens. The tissue is placed in Bouin's solution or formalin as soon as it is taken. Routine paraffin sections are prepared, and no attempt is made to use frozen sections for rush diagnosis of the tissue.

### Incidence and Types of Malignancies Diagnosed by Biopsy

The number of clinical visits and biopsies per year is shown in Table I. The increasing biopsy rate is the result of a broader interpretation of the indications for biopsy, as our staff have been impressed by their inability to differentiate clinically between cancer and benign cervical disease. Biopsies were made in only 6.9 per cent of the patients who attended the clinic in 1943. The incidence of biopsies has increased progressively to 28.6 per cent in 1948. In 1943, 18.8 per cent of the specimens showed malignant disease. The incidence of positive biopsies has decreased progressively to 5.7 per cent as the biopsy rate has increased.

One hundred sixty-five malignancies of the cervix—9.2 per cent of the total number of biopsies—have been diagnosed in the period of this study. Only those women with clear-cut carcinoma of the cervix are included. All cases in which equivocal pathologic lesions were present were eliminated from the series. Clinical records are available for analysis in 133 of the cases of carcinoma of the cervix. Thirty-two patients were seen only for a biopsy and were given further care elsewhere.

In each of the cases included in this series an invasive malignancy of the cervix was demonstrated in the pathologic sections. There were 160 cases of squamous cell carcinoma, four cases of adenocarcinoma of the cervix, and one primary sarcoma of the cervix. The importance of taking numerous sections of the tissue, which has been emphasized by Novak,[14] was frequently demonstrated in this study. As TeLinde has observed, neoplastic changes may

be present in several places in some cervices. In others, however, repeated biopsies were necessary before carcinoma was demonstrated. In one case, cancer was found in the operative specimen after a total vaginal hysterectomy; two previous biopsies of the cervix had failed to demonstrate a malignancy.

TABLE I. GENERAL INFORMATION

| | 1943 JULY-DEC. | 1944 | 1945 | 1946 | 1947 | 1948 JAN.-JULY | TOTAL |
|---|---|---|---|---|---|---|---|
| Outpatient visits | 763 | 1751 | 1982 | 2057 | 2311 | 1151 | 10,014 |
| Number of biopsies | 53 | 196 | 256 | 505 | 461 | 329 | 1,797 |
| Incidence of biopsy (per cent) | 6.9 | 11.1 | 12.9 | 24.5 | 19.9 | 28.6 | 17.8 |
| Number of cases of cervical carcinoma | 10 | 24 | 33 | 44 | 34 | 19 | 165 |
| Per cent of biopsies positive for carcinoma | 18.8 | 12.2 | 12.9 | 8.9 | 7.4 | 5.7 | 9.2 |

## Ages of the Patients

In general, the ages of the patients conform with those usually reported. However, six were under 30, and 39 (29.3 per cent of the group) were under 40 years of age (Table II). Correlation of the patients' ages with the clinical stage of the disease was not significant (Table III).

TABLE II. AGES OF PATIENTS WITH CERVICAL CARCINOMA

| DECADE | TOTAL |
|---|---|
| 20-29 years | 6 |
| 30-39 | 33 |
| 40-49 | 52 |
| 50-59 | 22 |
| 60-above | 20 |
| | 133 |

TABLE III. AVERAGE AGE OF PATIENTS IN EACH CLINICAL STAGE OF CERVICAL CARCINOMA (LEAGUE OF NATIONS CLASSIFICATION)

| | AVERAGE |
|---|---|
| Stage I | 44.2 |
| Stage II | 48.5 |
| Stage III | 46.3 |
| Stage IV | 44.7 |
| Average—133 cases | 46.4 |

## Symptoms

One hundred three of the patients had symptoms suggestive of pelvic malignancy (Table IV). In 86, excessive or abnormal bleeding was the presenting symptom; fourteen complained of pain; and in three patients the respective complaints were the presence of a visible tumor, fever, and incontinence of feces. It is significant that thirteen patients had no symptoms referable to the pelvis, and were referred because a small cervical abnormality was discovered in the course of a routine physical examination. Seventeen additional patients had noted only a mild leucorrhea which was not remarkable in any way.

TABLE IV. PRESENTING SYMPTOMS IN 134 CASES OF CERVICAL CARCINOMA

| PRESENTING SYMPTOM | JULY 1943-DEC. 1945 | JAN. 1946-JULY 1948 | TOTAL |
|---|---|---|---|
| Bleeding | 37 | 50 | 87 |
| Leucorrhea | 8 | 9 | 17 |
| Pain | 5 | 9 | 14 |
| None | 2 | 11 | 13 |
| Fever | 1 | 0 | 1 |
| Patient noted tumor | 0 | 1 | 1 |
| Incontinence of feces | 0 | 1 | 1 |

## Clinical Impression

One of the most important facts ascertained by the present study is the high percentage of error in the clinical impression of cervical disease (Fig. 1). Each patient who comes to our clinic is examined by an experienced gynecologist. In 104 of the 133 cervical carcinomas analyzed in this series a clinical diagnosis of carcinoma of the cervix was made or suspected. In 29 of the patients, 21.8 per cent, the lesions were considered benign. The number of patients with a clinically benign lesion in whom an accurate early diagnosis of cancer has been made as a result of routine biopsy has increased each year.

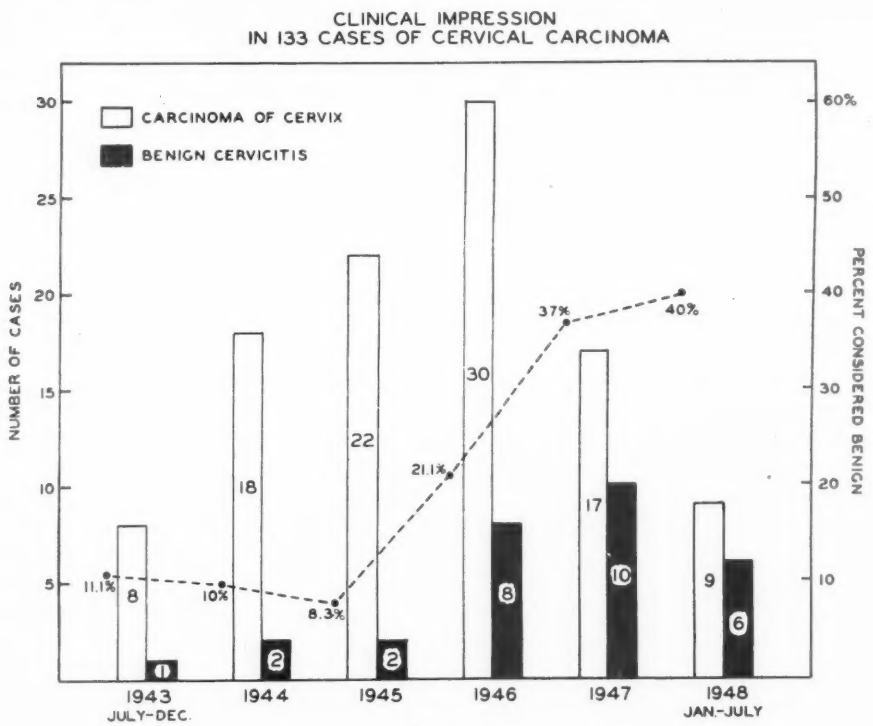


Fig. 1

## Clinical Classification

The extent of clinical involvement of the pelvis was recorded by the League of Nations classification in 117 cases (Fig. 2). We were not certain of the clinical stage of the lesion from the record in 16 cases seen by other services. In 33 (28.2 per cent) of the patients the cancer was strictly limited

to the cervix. In 26 patients (19.5 per cent) the total lesion was 2 cm. or less in diameter; in nineteen of this group the lesion was 1 cm. or smaller. Only 32 patients (27.3 per cent) had advanced involvement of the parametrium and adjacent pelvic organs and were in the third and fourth stages of cervical carcinoma.

In 1943, two-thirds of the patients had advanced clinical cancer. The steady trend toward the diagnosis of earlier lesions is shown in the analysis by years (Fig. 2). Although the actual number of advanced cases observed has not decreased, there has been a striking increase in the percentage of cases in which classification as Stage I or II was justified by the clinical findings (1943, 33 per cent; 1944, 53.3 per cent; 1945, 70 per cent; 1946, 91 per cent; 1947, 75 per cent; 1948, 73 per cent). While in 1943 only 33 per cent were classified as Stage I or II, more than 70 per cent of the cases during the last three years have been in these classifications. In 1947, fourteen (58.3 per cent) of the twenty-four new cases of cervical cancer were classified as Stage I.

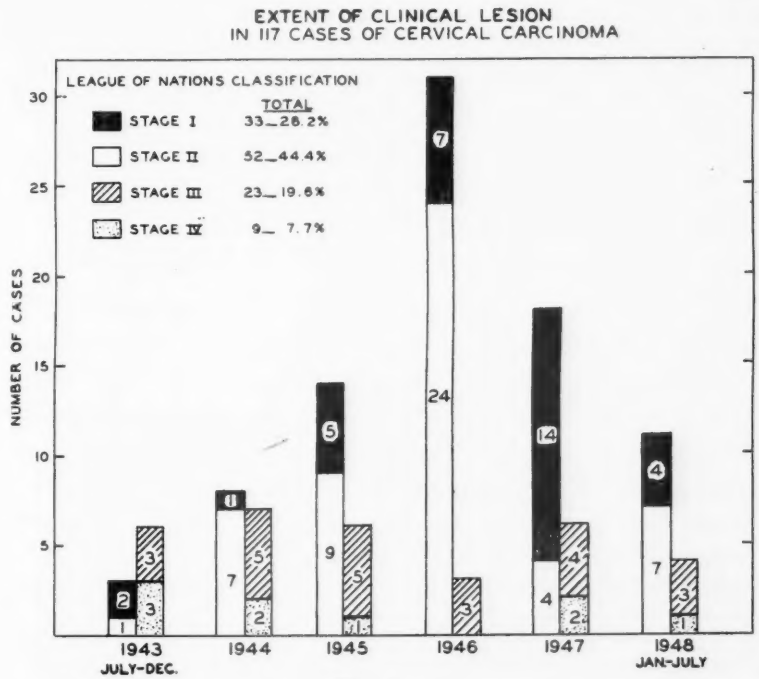


Fig. 2.

## Discussion

We feel that the patients in this series represent a selected group, because practically all of them were referred to the clinic by a physician. A full report is mailed to the referring physician concerning each case. As a consequence of this practice, there has been an increasing tendency upon the part of the referring physicians to send patients with apparently insignificant changes in the cervix to us for biopsy. This tendency is also strikingly evident in the collateral medical services of our outpatient department. The members of the hospital staff in surgery and internal medicine are acutely conscious of their inability to make a satisfactory clinical evaluation of the condition of the uterine cervix.

The effect of the widespread educational program on cancer is obvious in our area. The majority of the general practitioners are making careful physical examinations, and many patients are insisting upon pelvic examination when it is omitted. Our records include a number of patients who saw a physician for a general check-up or some incidental disease. One of the patients consulted a general practitioner for treatment of poison-ivy dermatitis, and a Stage I cervical carcinoma was found in the course of his examination.

Our observations have confirmed those of previous authors. Early cervical carcinoma can be diagnosed only by pathologic examination, and biopsy is the one decisive diagnostic procedure leading to recognition of early cervical cancer. No dependable clinical signs are available to us. The early lesion may be hard, normal, or soft in consistency. The presence of a granular surface or one which bleeds easily increases the likelihood that carcinoma is present, but is by no means a pathognomonic sign of this disease. A smooth, clean, intact cervix with a reddened area which we describe as "tomato blush" may be the site of early carcinoma.

Removal of a biopsy specimen from the cervix is a minor surgical procedure, and we believe that it should be included in the gynecologic consultation. It is performed easily as an office procedure with little or no discomfort to the patient. Little care of the biopsy wound is required, and complications are rare. The removal of the diseased tissue is effective treatment for many benign cervical lesions, and a therapeutic as well as a diagnostic result is obtained. In our clinic no professional fee is charged for taking a biopsy specimen. The pathologist receives a nominal fee from private patients for preparation and examination of the tissue.

## Summary

1. In the clinics of the Bowman Gray School of Medicine of Wake Forest College and the North Carolina Baptist Hospital a cervical biopsy is performed in every case in which the appearance of the cervix shows any deviation from the normal. The results of this policy over a five-year period have been reviewed. One thousand, seven hundred ninety-seven biopsies were taken during 10,014 visits, and 165 cases of cervical carcinoma were discovered.

2. Thirteen of the 165 patients with carcinoma of the cervix had no symptoms. In seventeen only leucorrhea was present. The remainder had other symptoms suggestive of genital cancer.

3. Of this series of patients, 72.7 per cent had Stage I or II involvement (League of Nations classification). In twenty-six cases the carcinoma was 2 cm. in diameter or smaller. Fourteen (58.3 per cent) of the twenty-four new cases observed in 1947 were classified as Stage I.

4. Twenty-nine cases of carcinoma were discovered which were clinically considered to be benign cervical disease.

5. Our policy of performing a biopsy in every case in which any abnormality of the cervix is observed has resulted in the diagnosis of increasing numbers of early cases of cervical cancer.

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## Discussion

DR. ROBERT L. FAULKNER, Cleveland, Ohio.—This paper describes a tried method for diagnosis of carcinoma of the cervix, available to everyone. The author in his study has about one in ten cervical biopsies positive for cancer. This is evidence enough that biopsy was done two or three times as often as by the average gynecologist. What he has done is apparently to assume that no cervical lesion is benign until proved so by microscopic diagnosis.

The only trouble with biopsy, as ordinarily done, is that it is "spot" diagnosis. Just as it is true that carcinoma of the cervix may be present without symptoms, so it is true that carcinoma may be present in a cervix without anything to see. In addition there is so often no investigation of the cervical canal where carcinoma may arise, and where it so often becomes extensive disease before detected.

It is probably wise to have no set method of performing biopsy. The method of making a spot biopsy matters very little just so it is made. Personally, I have never had much luck keeping a biopsy punch sharp enough to do much good and use a long handled tonsil knife and an Allis clamp. There is much of interest in the method of scraping the cervix as advocated by Schiller, Ayre, Novak, and others. This may be done with the ordinary scalpel or, as suggested by Novak, with a spoon sharpened on the edges. When put through the same process and mounted in paraffin as ordinary biopsy material, study is made much easier. In addition, because of dread of missing a carcinoma of the middle third of the cervix, I have frequently employed a very small curette to investigate the cervical canal above the point of external biopsy. This is particularly useful in normal-looking but bleeding cervical stumps. When the patient is in the hospital and a curettage is being done it must always be remembered to curette the endocervix, and these curettings may be saved separately from the uterine curettings, thus constituting in effect a fractional curettage. In rare instances conization, or in older women even amputation of a cervix may be necessary for adequate biopsy.

In addition to studying the cervix by biopsy, the author is right about another detail, the proper study of all biopsy material by paraffin section and the omission of attempts at frozen section diagnosis. In a very few institutions especially equipped for such preparations exceptions may be made, but generally speaking there is no great hurry, and paraffin sections in ordinary hands give a very much better over-all picture of the tissues removed.

There is no point to being reactionary about vaginal cytology until its place in the scheme of things is further shaken down. One minor point that is of some importance has to do with the financial support of such studies. So far such support has to be arranged for outside of a charge to the patient. When the cost of such an examination to the patient anywhere near approximates the cost of reading a biopsy specimen, it is no longer worth doing because one screening of diluted vaginal or cervical secretions, especially if negative, means nothing one way or another in cancer diagnosis.

DR. MORTIMER N. HYAMS, New York.—I am in full agreement with the statement that colposcopy has not proved of much advantage as a diagnostic aid in determining cervical

carcinoma in its early stage. However, the Schiller test can be of considerable help in conjunction with other procedures.

While cervical biopsy is a valuable diagnostic procedure and, in a large percentage of cases, gives definite confirmatory information leading to a correct diagnosis, I believe that in certain cases, in spite of properly carried out biopsy technique, some diagnoses will be missed. A negative biopsy report does not always spell safety for the patient. I recall a case of this kind in my own experience. A number of years ago, we had on our gynecological service at New York Post Graduate Hospital a patient about 38 years of age, with a chronic cervical infection, which we considered to be of the third-degree type. A biopsy was made and the tissue examined by a competent pathologist, who reported a chronic cervicitis. As this patient also had a lacerated perineum, she was advised to enter the hospital for perineal repair and plastic operation on the cervix. These operative procedures were carried out. Much to our surprise the pathologist reported a squamous cell carcinoma of the cervix. A further examination of the first cervical specimen taken preoperatively, proved negative for malignancy, while the tissue removed at operation was definitely carcinomatous. We had evidently removed tissue from a nonmalignant area. Similar findings have been reported by others. Since the experience just mentioned, it has been our custom never to depend on one piece of tissue, but to remove two or even three specimens from different areas at every cervical biopsy and to cut several sections from different parts of the block of tissue. It is obvious that an early carcinoma located just inside the external os, will not only be overlooked macroscopically but often missed when making a biopsy.

Vaginal smears and the more recent endocervical smear method of Papanicolaou, represent a decided advance in the diagnosis of early cervical carcinoma, but their value is sometimes underrated, because of diverse reports, often erroneous, following the smear examination. These unsatisfactory and often disappointing reports are due in many instances to the fact that the examination has been attempted by those inexperienced in the field, or by technicians not qualified by proper training in their interpretation. This is a highly specialized phase of laboratory technique and should be carried out by a competent pathologist, properly trained in this type of examination.

Long before any macroscopical changes are apparent in the cervical tissue with the advent of carcinoma, abnormal cells are often demonstrable in the vagina. Hence the extreme importance of vaginal smears in making our early diagnosis. While the final criterion is the determination of cancer cells under the microscope, I believe that vaginal smears are a very important link in the chain of tests which aim at the recognition of carcinoma of the cervix in its incipiency. In stressing the importance of vaginal smear examination, I recall the case of a woman 42 years of age, whose chief complaint was slight intermenstrual bleeding of several months' duration. Physical as well as pelvic examination was negative; routine vaginal smears were positive for carcinoma. The patient was admitted to the hospital and biopsy specimens were taken from several areas of the cervix, the uterine cavity as well as the cervical canal curetted; cervicouterosalpingograms were made. All tissue tests and x-rays were negative for carcinoma. Vaginal smears repeated on several occasions, still showed a positive reaction. The patient was given radium therapy. Vaginal smears taken at intervals since then have all been negative. Unfortunately, this patient was not subjected to hysterectomy to demonstrate the carcinomatous lesion. The value of smear examination has been confirmed by Meigs, Ayre, Warren, Pund and others. It is conceded that smear diagnosis should be supplemented by histological examination of cervical tissue to establish proof of carcinoma. Therefore, smears and biopsy should be made in every case with suspicious signs or symptoms. Schiller has emphasized that carcinoma of the cervix can be diagnosed before invasion occurs and has introduced the procedure of staining the cervix with an aqueous solution of iodine to reveal suspicious areas requiring biopsy.

Whether treatment should be instituted, based only on a positive cytologic report is open to question. If abnormal, cancerlike cells are found in the vaginal smear, every effort must be made to localize the primary site of involvement: biopsy of the cervix, cervical canal scrapings, as well as uterine curettage, to be repeated, should they prove negative.

Dr. Locke Mackenzie, cytologist at the New York Post Graduate Hospital recently reported a very interesting case. A virgin in her late thirties complained of menopausal symptoms for which she sought relief. General physical examination as well as pelvic examination was essentially negative. The cervix was of the conical type with no macroscopic evidence of pathology. Routine vaginal smear examination showed the presence of many abnormal cancerlike cells. Repeated smear examinations confirmed the findings. A total hysterectomy was done and examination of the tissue removed at operation revealed the presence of an early cervical-canal carcinoma.

Positive vaginal smears, despite a negative biopsy, should put us on guard and warn against delaying either radium applications or surgery, whichever may be indicated. Procrastination may be followed by an invasive carcinoma which could have been prevented by appropriate therapy.

The vaginal smear as a diagnostic aid cannot be passed by lightly with the statement that its usefulness is limited by the paucity of expert cytologists and that the test will not be generally available for many years. I believe it is an important aid whose ultimate value has not been discovered but whose possibilities are still under consideration and investigation.

DR. EMIL NOVAK, Baltimore, Md.—Like Dr. Faulkner, I find it rather refreshing to hear a paper on the early diagnosis of cancer of the cervix which is not based on vaginal cytology studies. You may gather from this that I am a bit of a reactionary on the question of vaginal smears, and, in the present state of our knowledge, I believe that one can still be a thoroughly competent gynecologist even though he has never done a vaginal smear. I have no criticism to make of the small group of competent cytologists who are exploring the possibilities of the method. As a matter of fact, it is this very group of investigators who have been emphasizing that the vaginal smears technique is of only supplementary nature, that it does not have the decisive value of the tried and true method of biopsy, and that its chief value, for the present, and perhaps always, will be as a screening method. However, vaginal cytology is not the immediate subject of the present discussion.

Reference has been made to the method of surface biopsy of the cervix which I have been urging as definitely superior to the smear method, or to the light cervical spatula scraping advocated by Ayre. The cervix in the vicinity of the junction of the two types of epithelium is sharply scraped or pared with a scalpel or two-edged spoon, yielding long strips of the whole epithelial thickness, thus giving a far more comprehensive and concentrated picture of the epithelial status than the highly attenuated one obtained from vaginal smears. A slightly oozing surface is left, but this is completely epithelialized within a matter of days. There is, of course, nothing original in the method, for such surface biopsy was recommended by Schiller and others many years ago, although it has not been practiced by many gynecologists. It is of obvious value where no suspicious lesion is present, and where the ordinary type of biopsy, even though multiple, might still miss a subclinical lesion.

In a recent case, the cervix showed only an innocent looking erosion, with slight vascularity and granularity at one angle. A wedge excision of the latter was done with also surface biopsy of the whole circumference. The former was completely negative for malignancy, but the surface strips showed typical preinvasive carcinoma. As the patient was in her forties, a modified Wertheim operation was done, and further studies of the cervix showed a very early invasive lesion.

My own interest in this method is not based entirely on its value in cancer diagnosis, but, also in the material which it will give us for the study of cyclical changes in the stratified squamous epithelium of the cervix. It is my impression that many of the milder degrees of so-called basal cell hyperactivity which have been stressed and probably overstressed as precusors of cancer are probably of cyclical or hormonal nature. This is further suggested by the remarkable pseudomalignant changes in the squamous epithelium which have been noted during pregnancy and are quite surely due to the large amounts of estrogen characterizing the latter.

DR. WILLIS E. BROWN, Iowa City, Iowa.—The present methods of treatment of cancer of the uterine cervix provide five-year survival rates ranging from 30 per cent to 40 per cent (University of Iowa, 39 per cent). While these results suggest that present forms of treatment are largely unsuccessful, such is not entirely the case; for almost 90 per cent of the patients seen when the lesion is confined to the cervix are alive and well at the end of five years. Apparently, then our methods of treatment are effective against cancer of the cervix but fail in the treatment of cancer that has extended beyond the cervix. The effectiveness of therapy is an indirect measure of our ability to detect and diagnose early cancer.

The essayist is to be congratulated on instituting routine biopsies of all lesions of the cervix, and the discovery of twenty-six unsuspected carcinomas. There are two points that I should like to make in this regard. While routine biopsy will discover many cases of early and unsuspected carcinomas in patients examined by the gynecologist, it is not applicable as a population screening procedure. Also, in 115 proved carcinomas found during the course of survey of 5,000 women, the initial biopsy failed to detect the cancer in 6 per cent of the cases.

We have attempted to extend the advantages of early diagnosis to the general population by the use of routine vaginal smears. The techniques commonly advocated for obtaining vaginal cells are not suited to population survey. We devised a method so simple that nurses or technicians can obtain smears from about twenty women an hour. The effectiveness of pelvic examination, biopsy, and vaginal smear in the detection (not diagnosis) of genital carcinoma has been evaluated.

We studied 5,314 vaginal smears from three groups of women over the age of 30 years—women entering the University Hospitals regardless of the service or complaint, patients in state mental hospitals, and a group of women from a near-by county who volunteered for the study.

Twenty-five hundred women over the age of 30 admitted to the University Hospitals had routine cytologic studies, pelvic examinations, and biopsies, when indicated, for the detection of genital cancer. Most of the pelvic examinations were done by the resident staff, the smears were examined in a special cytology laboratory, and the biopsies were diagnosed by the Department fo Pathology.

Following this detailed study of the University Hospital patients, the procedure was employed in two state mental hospitals, and on a volunteer basis in a near-by county. The vaginal smears were read and when abnormal cells were found, the patients were referred for repeat smears and careful gynecologic examination including biopsy, when indicated. The use of this method singles out those patients who may have asymptomatic genital malignancies. In this survey, one unsuspected carcinoma was found in each 300 to 400 women studied. This approach of population survey can single out those apparently well women who need critical study.

While biopsy is the recognized method of establishing the diagnosis of cancer, it was found wanting in the detection of early and unsuspected cancer. Some women in whom cancer was subsequently shown to be present were thought to be free of cancer on the first clinical examination or biopsy. The presence of abnormal cells in the vaginal smear led to further examination and repeat biopsy. Frequently, it required two or three biopsies to establish the presence of cancer first suspected by the cytologic study.

The effectiveness of these routine methods of detection of genital cancer is shown against the final diagnosis. Each of the three methods shows considerable error in the detection (not diagnosis) of cancer. A statistical analysis of this material indicated that the value of the smear method was greatest in detecting early and preclinical lesions, and was least in advanced or sloughing malignancies. The effectiveness of pelvic examination and biopsy in detecting uterine carcinoma was found to be just the reverse.

In addition to the use of biopsy before treatment of the cervix is instituted, we should like to urge that *all* women seeking medical care be given the benefit of routine vaginal smears. This will not only improve the results of routine examinations but will help select patients for biopsy.

DR. OTTO H. SCHWARZ, St. Louis, Mo.—There is no question that the routine use of the Schiller test, the colposcope, and recently the study of vaginal smears are all valuable adjuncts in the diagnosis of cervical cancer; but they in themselves are not enough. This latter procedure will in my opinion also become commonplace, but a biopsy will also be needed for confirmation. Dr. Faulkner used the term "spot" biopsies; discussion of the slides usually follows with the remark, "Let us get more tissue." In my opinion in most instances where biopsy is considered, the lesion is such that if it should be benign it would definitely need treatment. Perhaps this would be considered radical, but I feel under these circumstances a good cervical conization with light coagulation gives plenty of tissue for examination; if benign it cures the lesion, if malignant, no harm is done. Graves has shown in a large series, years ago, where Sturmdorf operations had been done the incidence of cancer was most strikingly reduced, and the same holds for conization as has just been shown by Robert Crossen in a very large series. Even with all this, the diagnosis of carcinoma is not always clear-cut, suggestive let us say; under those circumstances, the patient should receive the benefit of the doubt, and as Halban has so well put it some years ago, "Nicht Karzinom, aber besser heraus," and we might add "or treated."

DR. LOCK (Closing).—The patients in this series represent a selected group because they are practically all referred to the clinic. In many of them a small lesion was noted by the general practitioner in the course of a general physical examination. Each referring physician is sent a full report of the result of the examination of his patient during the period of our study. As a result they have learned that we cannot differentiate cervical cancer from benign lesions by a clinical examination, and have in turn referred more and more patients to the clinic for cervical biopsies.

We take numerous pieces of tissue as Dr. Hyams suggests. A curettement is recommended for each patient who has appreciable bleeding after the passage of a uterine sound. The endocervical tissue is kept as a separate specimen from those obtained from the uterine cavity.

# ECTOPIC PREGNANCY, MORTALITY AND MORBIDITY FACTORS*

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IN 1922, Graffagnino[1] reported a study of 186 cases of ectopic gestation treated in Charity Hospital, New Orleans, during the years 1908 to 1920. He established that 23 of the cases succumbed (12.3 per cent). Commenting on this mortality rate, Graffagnino stated, "[It] is unusually high compared with 4.3 per cent at Hopkins, not quite 1 per cent at Women's Hospital, and 8 per cent at Cook County Hospital. As is to be expected, the highest death rate prevails at the two general hospitals, where the patients are of a lower social status, where it is more difficult to secure adequate histories to justify very early interference, in cases that could be saved, and where a greater number of patients were admitted moribund." In 1935 Tyrone, Romano, and Collins[2] reviewed 309 cases of ectopic pregnancy, hospitalized at Charity Hospital, New Orleans, during the period 1924 to 1934, and found that there were 36 deaths (11.6 per cent), in which the cause of death was directly attributable to this lesion. In 1938 Graffagnino, Seyler, and Bannermann[3] surveyed the cases of eccyesis at the same institution admitted during the period 1919 to 1937. Of 445 cases available for study, 51 deaths were encountered (11.4 per cent). In the period 1906 to 1936, therefore, the mortality rate from extrauterine pregnancy fluctuated between 11.4 per cent and 12.3 per cent. Indeed, there was very little improvement in the years 1920 to 1936 as compared to the period 1906 to 1920.

A study by the authors[4] of cases of extrauterine fetation entering Charity Hospital, New Orleans, during the period 1937 to 1945, revealed a mortality rate of 2.7 per cent, while from 1945 to 1948 the death rate was reduced to 1.7 per cent (Fig. 1). The factors involved in the precipitous decrease in the mortality rate from ectopic pregnancy at this institution during this eleven-year period as compared to the death rate from 1905 to 1937, inclusive, form the basis for this presentation.

## Facilities

Not a small factor in the lowering of the mortality rate was the opening of a new Charity Hospital building in July, 1937. Prior to that time the main portion of the hospital consisted of an out-dated structure, much overcrowded and not conducive to the best study of, or care of, patients. It was not unusual for two patients to have to share the same bed. Outpatient facilities

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were crowded and only three examining tables were available for a clinic of well over a hundred patients. Undoubtedly inaccurate diagnoses were made in a physical setup of this type that would not have been made had more adequate facilities been available. The new structure contains adequate beds, treatment rooms, and laboratory facilities, and a larger number of observation rooms. The latter are used for the direct admission of emergency cases and are air-conditioned, not a small factor in subtropical climates. Here a study of all acute diagnostic problems can be carried out thoroughly, comfortably, with adequate diagnostic aids, and immediate consultation from all divisions of the hospital staff, resident or visiting. An adequate number of residents are assigned to the division as well as full-time admitting physicians and in this manner emergencies are better cared for.

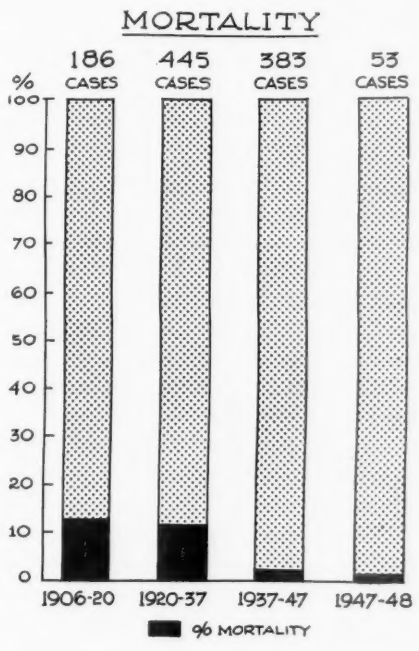


Fig. 1.

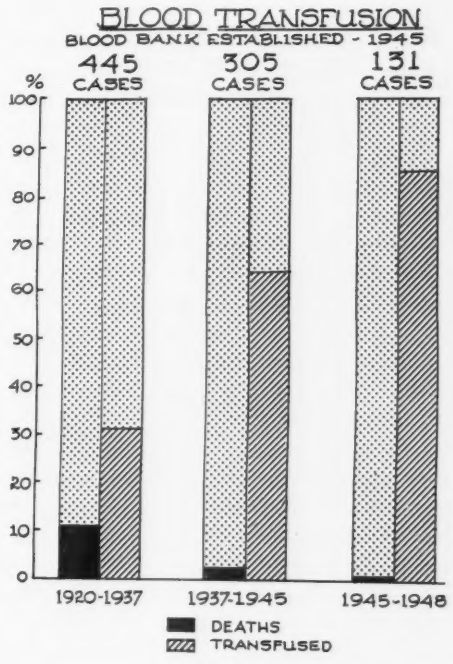


Fig. 2.

## Staff

In 1937 residencies in the various specialties were established at Charity Hospital. Prior to this time the "house officer" system was in vogue, there being but two types of "house officer," i.e., medical and surgical. The surgical group cared for obstetrics and surgery while the medical group cared for other cases. The visiting staff were divided into specialty sections. Needless to say, the establishment of residencies in the various specialties, with strict designation of duties, has had much to do with the marked lowering of the mortality rate, especially since consultations among the different groups are easily sought and obtained. At about the same time, the hospital staff was reorganized and more wards brought under university supervision. For a long period there was only one university with a teaching service at Charity Hospital, now the hospital utilizes the services of two medical schools to supervise the care of 80 per cent of its patients. This has doubled the teaching

staff and resulted in the training of a larger number of men, in the various specialties, many of whom have remained on the staff of the hospital following completion of their residencies and this in a large part is responsible for the decreased mortality and morbidity rates.

### Blood, Plasma, and Oxygen

There is no doubt that when a patient suffers from hemorrhage, the most efficient method of combating shock and other complications is the administration of blood in adequate quantities. Lyons and his workers[5] have emphasized the importance of blood volume, not only as regards oxygen-carrying capacities but in combating infection. Furthermore, the demands by the body on protein to form hemoglobin, before the protein can be utilized to build body tissue, require the replacement of blood lost if good wound healing is to be expected. The liberal use of blood transfusions in cases of ectopic pregnancy is necessitated not only to combat shock but to reduce the possibility of infection, aid in the conquest of infection, and enhance the patient's chances of having a wound heal without dehiscence. Blood not only saves lives, it reduces morbidity. In the absence of available blood, plasma is a good substitute. The improvement noted in our mortality rate is in a large part due to the availability of plasma in 1938, dried plasma in 1944, and the establishment of a blood bank in 1945. In 1938 Graffagnino stated, "We feel hesitant about reporting the small number of transfusions which were given when we realize what a valuable therapeutic measure it is in this type of case. However, it must be appreciated that we are dealing with patients from all over the state of Louisiana, whose relatives are often difficult to contact for donors and when contacted are reluctant to give blood." This statement still holds true in some respects but the establishment of a blood bank in 1945 eliminated most of the difficulties we formerly experienced in obtaining blood.

From 1920 to 1937, only 31.5 per cent of the patients admitted with ectopic gestation received a blood transfusion and the mortality rate was 11.5 per cent. From 1937 to 1945, 64 per cent of the patients were transfused and a mortality rate of 3.3 per cent recorded. In the period, 1945 to 1948, following the establishment of a blood bank, 86 per cent of the patients with eccyesis were transfused, and the mortality rate decreased at the same time to 1.3 per cent (Fig. 2). In the years 1937 to 1945, 305 cases of ectopic pregnancy were observed at Charity Hospital and 354 pints of blood utilized for their care, an average of 580 c.c. per case admitted or an average of 750 c.c. per patient transfused. Since the establishment of the blood bank in 1945, to Jan. 1, 1948, 131 cases of ectopic pregnancy were admitted and 260 pints of blood administered to these cases, an average of 990 c.c. per case admitted, or 1,150 c.c. per patient transfused. Twice as much blood per patient admitted was used in the latter period as compared to the former. Not only were transfusions given, but in most instances as much blood, or more, than that found in the abdomen was utilized. In no instance was autotransfusion used. In a few cases overzealous and too rapid administration of blood, plasma, and/or electrolytes has resulted in transient overloading of the circulation and pulmonary edema. No deaths resulted, but in our efforts to replace or maintain blood volume the possibilities of introducing such an undesirable complication must be constantly kept in mind. At Charity Hospital the establishment of a blood bank and the increased use of blood transfusion in the therapy of eccyesis is a major factor in lowering the mortality and morbidity resulting from this pathological process.

A fair number of patients entering Charity Hospital with tubal pregnancies are admitted in shock or develop shock soon after admission. Graffagnino,[3] commenting on his study of 445 cases of ectopic gestation admitted to Charity Hospital between the years 1919 and 1936 states, "There were 51 deaths in this series of cases. Twelve patients died before operation, five died on the operating table, and 34 died after operation. Of the patients who died, 35.3 per cent were admitted in shock, 25.4 per cent in poor condition, 17.7 per cent in fair condition and 21.4 per cent in good condition." Since 1937, 14 per cent of the cases have had shock on admission and an additional 7 per cent have developed shock soon after admission. Roughly, one out of every five patients was in shock before operation was started. The early administration of blood and/or plasma and early operation are musts in the treatment of intraperitoneal hemorrhage, but so, also, is the early and continuous administration of oxygen. Oxygen should be administered until the patient's blood pressure and pulse have been stabilized to or near to normal. Body cells, especially those of the more specialized organs, are sensitive to a deficient supply of oxygen. This is especially true of the pituitary gland of the pregnant female.[6] The administration of oxygen has a twofold purpose, first, to help prevent death and, second, to help prevent those who do survive from being "human vegetables." Since 1937, the availability of, the generous supply of, and the early and continuous use of oxygen as a routine measure to patients in shock, has, together with blood transfusion and early operation, resulted in a marked lowering of the number of patients failing to survive operation.

Thirty-nine operative deaths recorded in the 51 deaths in Graffagnino's series were due primarily to hemorrhage and shock. In the twelve deaths that occurred since 1937, only two have been due to postoperative shock, even though approximately the same number of cases per year were admitted in this period in a state of shock or developed shock soon after admission, as is recorded in Graffagnino's series. There was no correlation between the amount of blood used per patient and the postoperative stay of the patient. This at first may seem paradoxical but in reality means that patients requiring transfusion were transfused in proper quantities, so that fewer complications developed and the postoperative stay was no longer than those in whom blood transfusion was thought to be unnecessary.

## Diagnosis

Ectopic pregnancy presents a variety of signs and symptoms. None are constant. Certainly, in a patient giving a history of a missed period followed by sudden abdominal pain, while working or straining at stool, showing signs and symptoms of shock and in whom one is able to palpate a tender abdomen, tender cervix, and doughy mass in the cul-de-sac, the diagnosis is not difficult. However, unfortunately, very few cases fall into this category. In the majority of cases the symptoms and signs follow no set pattern.[4]

In this series, from 1906 to 1920, the diagnosis was mentioned on admission to the hospital or operating room in 45 per cent of the cases. From 1924 to 1935, in only 63 per cent of the cases. From 1937 to 1942 in 70 per cent of the cases. From 1942 to 1947, it was mentioned in 83 per cent of the cases, whereas in 1947 ectopic pregnancy was mentioned in 94 per cent of the cases. The absolute diagnosis of ectopic pregnancy, that is, an unequivocal diagnosis without mention of any other pelvic lesion was 40 per cent in the period of 1906 to 1920, 60 per cent in 1924 to 1934, 55 per cent in 1937 to 1942, 63 per cent in 1942 to 1947, and 74 per cent in 1947 (Fig. 3). Coincident with the

drop in mortality rate there has been a decrease in the time from admission to operation and also in postoperative stay. Certainly any diagnostic procedure that is fairly specific should help. We do not for one moment doubt that better facilities, increased trained personnel, and blood and oxygen have been important cogs in lowering the mortality and morbidity rate on our service but we also believe that the early routine use of cul-de-sac puncture in all cases suspected of having eccyesis has been one of the more important factors involved. The diagnosis is established earlier, with certainty, and operation is performed sooner. We have not seen any disadvantage or complications from the procedure. We believe that ectopic pregnancy should be treated by immediate operation as soon as the diagnosis is confirmed.

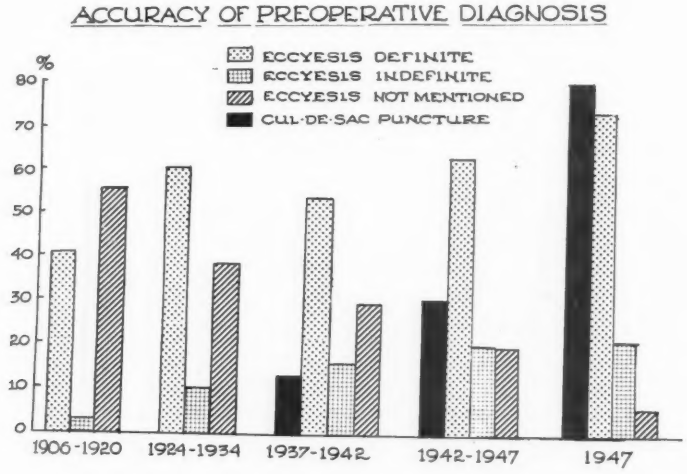


Fig. 3.

From 1920 to 1937 only 7 per cent of the patients were operated upon within three hours of admission and less than 30 per cent within 24 hours. Gradually the number of patients operated upon soon after admission increased until, in 1947, 60 per cent of the patients admitted were operated upon within three hours and 83 per cent within 24 hours (Fig. 4).

Immediate operation was made possible by the early specific diagnosis of intra-abdominal bleeding. Earlier diagnosis of intra-abdominal bleeding in turn was accomplished by the almost routine use of cul-de-sac puncture in all cases suspected of having eccyesis. Many of our staff in former years were certain that they could ascertain by vaginal examination the difference between blood in the cul-de-sac, either encysted or not, and pus or serous exudate. This is possible in many but not all cases. Routine examination of exudate in the cul-de-sac by means of needle puncture has led to the diagnosis of many cases of unsuspected ectopic pregnancies, and the discovery of pus or serous exudate in many cases where extrauterine gestation was suspected or believed to exist without doubt. The procedure is now used routinely on our service. True, in a few instances cases of unruptured tubal pregnancy have been missed and false positive or false negative punctures have been encountered but in no instance has a death resulted. The very fact that cul-de-sac puncture has been utilized in cases of unruptured ectopic gestation means that the possibility was in mind and these patients were either held

in the hospital for observation or told to return home but on the first sign of increased pain or bleeding, or feeling of faintness to return immediately. Moreover, all of these patients have their blood typed, cross-matched, and the Rh factor determined, in order that, if an ectopic pregnancy exists and has not been diagnosed, when rupture does occur blood will be available immediately. The possibilities and potentialities of culdoscopy in the latter types of cases are being explored on our service by two of us (W. D. and D. B.) but as yet no specific answer as to its value has been crystallized in our mind.

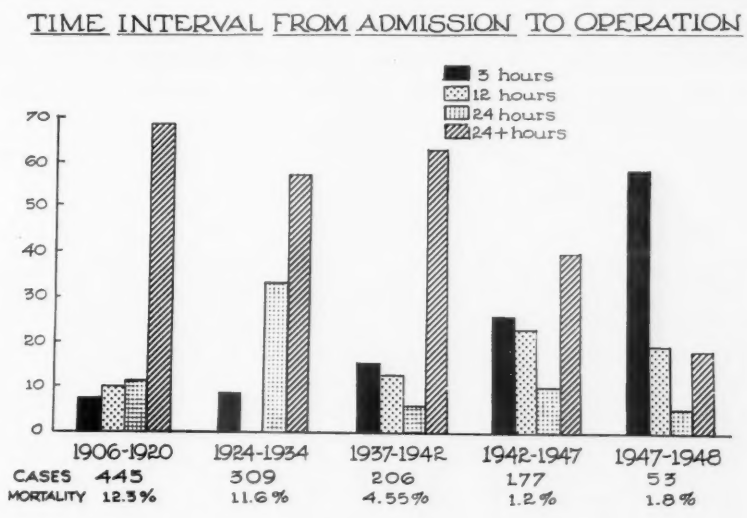


Fig. 4.

We have not used, though many large clinics do, colpotomy in the diagnosis or therapy of ectopic gestation. Colpotomy is used by us only when an abscess points in the cul-de-sac, whether the abscess is an infected hematoma or not. Early diagnosis is a very important factor in reducing the mortality and morbidity arising from ectopic pregnancy and exploration of the cul-de-sac either by needle puncture, culdoscopy, or colpotomy accomplishes this end.

## Operation

Early diagnosis and early operation should mean decreased mortality and morbidity and shorter hospital stay. Our procedure is to operate upon cases of tubal pregnancy as soon as the diagnosis is established and the operating room can be made ready. Patients in shock or near shock are administered oxygen and transfused as soon as grouping, cross-matching and Rh typing can be performed. Whether the patient is in shock or not the operation is begun as soon as possible. We do not believe that we accomplish anything by transfusing a patient and having the blood eventually find its way into the peritoneal cavity. In intraperitoneal hemorrhage the bleeding vessel must be ligated. In eccyesis we are dealing with shock from hemorrhage and the patient will not recover from shock until the source of bleeding is controlled. If the source of bleeding is not controlled surgically, she probably will succumb. Of the 88 fatal cases of tubal gestation occurring at Charity Hospital from 1906 to 1948, twenty (12 per cent) died from intraperitoneal hemorrhage and shock without any operative procedure having been undertaken. Cases of eccyesis can and do hemorrhage to death within the peritoneal cavities and

are emergencies. Blood transfusion without immediate operation is no guarantee that the patient will survive until "she is a better operative risk." No one should be lulled into a sense of false security simply because transfusion has been started. We have seen patients die of ruptured tubal gestation while being "prepared for operation with blood transfusion."

## Operative Procedure

The objective in the surgical management of ectopic pregnancy is to control intra-abdominal bleeding. Once this has been accomplished, removal or reconstruction of any organ or organs is potentially hazardous to the patient and in each case where such is contemplated the gravity of the measure or measures projected must be carefully considered by the surgeon. The seriousness of the incidental pathology, the condition of the patient, the amount of blood encountered in the abdomen, the quality of the anesthetic, the availability of compatible blood, and the extended scope of the projected operation must be carefully weighed. The procedures utilized in 424 cases of ectopic gestation operated upon from Jan. 1, 1937, to Jan. 1, 1948, are outlined in Table I. In no case can any of the fatalities encountered in this period be ascribed to surgical procedures used in addition to that necessary to control hemorrhage. It is re-emphasized, however, that in the vast majority of cases the operative procedure should be limited solely to the measures necessary to control the hemorrhage. Unilateral salpingectomy or salpingo-oophorectomy was the procedure of choice in 76.6 per cent of the 424 cases operated upon. One hundred seventeen surgeons, the vast majority residents, managed the cases in this series.

The anesthetic administered should be determined by the condition of the patient. Seventy of the 424 operative cases had spinal anesthesia. The remainder were anesthetized by ethylene, cyclopropane, or ether following gas induction. In no instance could a death be attributed in any way to the choice of anesthetic.

TABLE I. OPERATIVE PROCEDURE AND MORTALITY

| CASES | | SURVIVED | DEAD | TOTAL |
|---|---|---|---|---|
| Unilateral salpingectomy | | 134 | 3 | 137 |
| Bilateral salpingectomy | | 16 | 0 | 16 |
| Salpingo-oophorectomy | | 189 | 0 | 189 |
| Hysterectomy | | | | |
| Subtotal | 47 | | | |
| Total | 14 | | | |
| Vaginal | 4 | | | |
| | | 65 | 0 | 65 |
| Salpingectomy and suspension | | 20 | 1 | 21 |
| Not operated upon | | 0 | 8 | 8 |
| | Total | 424 | 12 | 436 |

Incidental appendectomy—42 cases—no deaths

## Postoperative Care

The reduced postoperative stay and decrease in morbidity and mortality not only reflect better preoperative and operative care but improved postoperative care as well (Fig. 5). Since 1937, chemotherapeutic agents and antibiotics have been added to our armamentarium. In addition a better understanding of adynamic ileus and the postoperative physiologic requirements of these patients has done much to hasten recovery. Patients in whom a large amount of blood is found in the abdomen usually develop a postopera-

tive ileus, no matter how gently the operation is performed or how little the pelvic organs are disturbed. The prophylactic use of Wangensteen suction for forty-eight to seventy-two hours in such cases has done much to insure rapid and complete recovery. Since 1937, in 436 cases it was found advisable or necessary to decompress 51 patients (10 per cent) either prophylactically or because of postoperative ileus. The efficacy of this policy aided by the early and judicious use of chemotherapeutic agents and antibiotics, when fever developed postoperatively, is established in that only two patients died from peritonitis in the period 1937 to 1948. Both these patients had peritonitis on admission. In Graffagnino's series, 1906 to 1920, thirteen of twenty-three deaths (57 per cent) were found to be due to peritonitis or "toxic ileus."

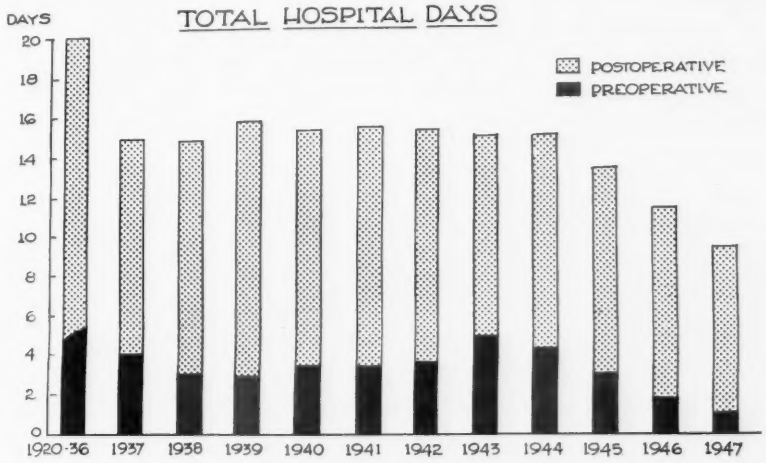


Fig. 5.

Evisceration of wounds most often occurs in malnourished, anemic patients, who, besides being depleted in protein and vitamins (especially vitamin C), develop distended abdomens and/or severe coughs. The prevention of, or early treatment of, adynamic ileus by the prophylactic or therapeutic use of Wangensteen suction; the liberal use of blood transfusion to replace lost blood volume and to lessen the demands on administered protein to produce hemoglobin and thereby increase available protein for fibroblastic production; and the intravenous administration of vitamin C and protein hydrolysates until the patient can tolerate food by mouth have been of inestimable value in that no case of evisceration, irrespective of type of suture material or type of wound closure, has been observed since 1937. True, five cases of the 436 (1.2 per cent) had some separation of the skin edges of the wound and in some the subcutaneous fat tissue separated, though none were severe enough to require secondary suture nor was fascial separation noted.

Wound infection was noted in 9 per cent of the cases operated upon since 1937. Phlebothrombosis, thrombophlebitis, or suppurative pelvic thrombophlebitis have not developed in any case observed since 1937.

## Deaths

Of the twelve patients who expired, eight died without benefit of surgery. Death resulted from cerebral apoplexy in one case of a 6 months' intrauterine gestation, and an old, inactive, tubal pregnancy was an incidental finding at

autopsy. The remaining seven patients died of massive intraperitoneal hemorrhage. Three of these expired within a few minutes following their arrival at the hospital. In all, procrastination on the part of the patient and not of the physician was responsible for the demise. Of the remaining patients who expired without surgical therapy one died in the admitting room after remaining there one hour and forty-five minutes without receiving blood or being prepared for surgery. Another died of shock en route to the operating room five hours after admission and, although the admitting diagnosis was correct, blood was not available for this patient. Because of inaccurate diagnosis, two others died ten hours and forty-eight hours, respectively, following admission, even though repeated transfusions were utilized in the latter. These four cases we consider to have been preventable deaths. Of the four patients who died following operation, two expired shortly after surgical therapy. Both of these were admitted, in extremis, their abdomens filled with blood and though they received prompt, thorough management, the outcome was fatal. Another patient expired twenty days after operation from intestinal obstruction. One patient had peritonitis resulting from an infected tubal pregnancy on admission and died shortly after laparotomy. Though some of these deaths were preventable in many they were the result of the patients' own procrastination in seeking medical care and resulted in their being admitted in an extremely serious state or moribund condition.

## Conclusions

1. The mortality rate from ectopic pregnancy in the years 1906 through 1936 fluctuated between 11.4 per cent and 12.3 per cent. From 1937 to 1945, 2.7 per cent fatalities were encountered. In the years 1945 to 1948, a further reduction to 1.7 per cent was accomplished.

2. Better physical facilities, the establishment of a residency system, and improved educational programs were instrumental in lowering the mortality and morbidity.

3. The establishment of a blood bank with the subsequent increased availability and use of blood is a major factor in the better results observed.

4. A better understanding of shock and postoperative physiologic requirements is reflected by the lowered number of fatalities and complications.

5. The increased use of cul-de-sac puncture and aspiration has increased the percentage of accurate and earlier diagnosis and is another major factor in the betterment of results obtained.

6. Ectopic pregnancy is an emergency. As soon as the diagnosis is established the pathological process should be treated by immediate surgery.

7. No other surgical procedures should be performed except that necessary to control the intra-abdominal hemorrhage, unless the patient is in excellent condition.

8. In cases suspected of having an unruptured ectopic gestation the patient should have her blood group and Rh type determined in order that should eccyesis be present and rupture ensue valuable time will not be lost in administering blood.

9. Many fatalities result from tubal pregnancy that might not have occurred had the patient sought medical care earlier.

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## Discussion

DR. FREDERICK J. LYNCH, Boston, Mass.—It is stated that extra-uterine gestation occurs once in every 300 pregnancies and a gauge of its importance as a cause of maternal mortality is evident in glancing at the statistics reported by Williams and Corbit of Philadelphia. In the ten-year period 1931 to 1940 it caused every eighteenth death in Philadelphia, every sixteenth death in New York City, and every twelfth puerperal death in Chicago.

One factor which influences the mortality statistics in any series of cases, and over which we have little control, is the all-important interval between the occurrence of the rupture or abortion and the time of entrance to the hospital, caused by tardiness on the part of the patient to call the doctor and the reluctance of the patient or indecision of the attending physician to have immediate hospitalization.

As Dr. Collins points out, there are two main types of cases, the typical and atypical, the typical accounting for 40 per cent of the cases and atypical 60 per cent. The former requires no diagnostic acumen but it is the latter that causes difficulties, and the delay for observation is the factor that results in trouble and causes the morbidity and mortality figures to mount, in any series. These atypical cases frequently are associated with a heterogeneous group of signs and symptoms which tend to raise the question in the mind of the physician of things other than an extrauterine pregnancy. The one note, however, that seems to sound through all these bizarre groups of symptoms is a woman exposed to pregnancy, who has menstrual irregularity in conjunction with pelvic pain, and a history and physical examination which are equivocal. This patient should be promptly hospitalized and subjected to the routine workup as outlined by Dr. Collins and immediately operated upon as soon as the diagnosis is established.

Although not mentioned by Dr. Collins, we have found that the biologic test—either an Aschheim-Zondek or Friedman—is helpful but the results must be interpreted. A positive test is an important addition to the diagnostic data but does not exclude the possibility of an atypical interrupted intrauterine pregnancy. It should be remembered that the test determines the presence of live trophoblast from which the anterior pituitary-like substance causing the positive test is produced. It must also be realized that false positives can be caused, rarely, by chorionepithelioma, leiomyosarcoma, corpus luteum cyst, and granulosa cell carcinoma. If the trophoblastic tissue has disintegrated and disappeared, the test will be negative, a condition which occasionally obtains in the presence of an old ruptured extrauterine pregnancy and occasionally even in recent ones. The positive biologic test can be of distinct value in arriving at the diagnosis but only when correlated with, and supported by, the other signs, symptoms, and findings of ectopic pregnancy. A negative test in the presence of a doubtful diagnosis may occasionally justify temporizing.

Also, a falling blood picture which seems to be incommensurately lower than the amount of external bleeding is extremely suggestive of hemorrhage into the abdominal cavity or extravasation into its tissues, and the presence of slight icterus in these patients is an almost infallible sign of hemorrhage into the peritoneal cavity.

Unquestionably, the most valuable single diagnostic aid is cul-de-sac aspiration or colpotomy. The patient, in whom an extrauterine pregnancy is a possibility, should have a needling of the posterior cul-de-sac using a large size needle—a needle which will permit the passage of fibrin and small clots. The presence of old blood in the barrel of the syringe is considered as positive evidence and its absence a negative test for extrauterine pregnancy. The old blood is identified by its characteristic brownish color, the lack of viscosity and its inability to clot. If blood is not found and the diagnosis is still in doubt the posterior cul-de-sac may be incised and each tube examined separately.

Burch and Seitchik report 37 cases suspected of harboring an extrauterine and in which cul-de-sac puncture was done; there were no false negatives and two false positives—one an adenocarcinoma of the cul-de-sac, and the other a ruptured Graafian follicle. In the series of cases they reported the test was 94.6 per cent accurate which compared very favorably with a correct diagnosis rate of 65 per cent in 34 cases in which the diagnosis was arrived at by the other usual clinical and laboratory means.

There has been a steady improvement in the mortality statistics associated with extra uterine pregnancy throughout the country. This has unquestionably been a part of the general improvement in all operative figures and is also probably a reflection of the immediate availability of appropriate blood, the vast improvement in the choice and administration of suitable anesthetics, and a more or less standard order of procedure as to the surest and most expeditious manner of arriving at the diagnosis.

DR. COLLINS (Closing).—Time did not permit me to make reference to the work of Dr. Frank Whitacre of Memphis in the study of blood hemachromogen in ectopic pregnancy. I think Dr. Whitacre has developed a very valuable diagnostic test, applicable not only to ectopic gestation, but to any case of intra-abdominal bleeding. We are very much impressed, even though we have only a small series, so far 40 cases, with the results obtained.

One thing we did not bring out was our management of the suspected unruptured ectopic. These patients are all matched and typed so that if the diagnosis is correct and they do rupture, we can give them blood immediately.

# KNOW THE PELVIS*

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*(From the Woman's Hospital of New York)*

KNOW THE PELVIS is a challenge to clarify our knowledge of the supports of the genital organs. By a simple model, one can clearly show where the damages of labor occur. Such information will point the way to an improved restoration of position and function, of organs long partially disabled.

Blood vessels, nerves, lymphatics, and pelvimetry are not included in this paper, nor are sinuses, fistulas and other pathologic conditions.

Backache, prolapse of organs, incontinence of urine and feces, poor voiding and evacuation are all sequelae of: (a) subinvolution of the uterus with or without retroversion; (b) infection of the cervix, and, (c) hidden injuries during labor. The pelvic organs (uterus, cervix, ovaries, tubes, bladder, urethra, vagina and rectum, anus and levator muscles) are all suspended from the white lines and their extensions along the ischiococcygeal ligaments over the coccyx.

This supporting body can be represented by a band and the attached structures can be divided into five superimposed separable layers (Fig. 1). Each of the four upper layers consists of a part of, or the whole of, an organ, held in position by supports which consist of connective tissue alone or connective tissue mixed with smooth muscle only (Fig. 2). One end of this support is attached to the white line and the other to the individual organ. The fifth and lower layer consists entirely of striated muscles. They have their origin in the white lines on each side and their insertions into or near the sagittal line of the pelvic floor and they move the urethra, the vagina, the perineal body, the sphincter ani, the raphe, or the coccyx either in separate units or in concert. This structure anatomically is the levator ani muscle.

*Layer 1.*—Comprises uterus, bladder, ureters, ovaries, and tubes. They are covered and supported by fascia endopelvina, of thickness to vary the strength necessary to accomplish delivery of the fetus without dislodging the organs. The round, uterosacral, and pubovesical ligaments are not attached to the white lines. This fascia endopelvina is attached to the white lines and their extensions, and makes an almost complete diaphragm between the abdominal cavity above and the extraperitoneal cavity below. It is completely covered with peritoneum.

*Layer 2.*—Comprises a cross section of the cervix and its supports. The outer half of the support coming from the white lines is entirely connective tissue, while in the inner half the connective tissue becomes increasingly more smooth muscle and less connective tissue, until at the cervix the support is predominately muscle. The cervical support makes a shelf for the bladder, the ureters, and the uterine and vesical blood vessels.

*Presented by invitation at the Fifty-Ninth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 9 to 11, 1948.

*Layer 3.*—Comprises a cross section of the cervix, the vaginal canal, and the vaginal orifice with its attachments to the levator muscles. The vaginal support is connective tissue coming from the white lines and their extensions and inserts itself into the vaginal wall. The vagina does not have to depend on the bladder, the cervix, or the rectum for support.

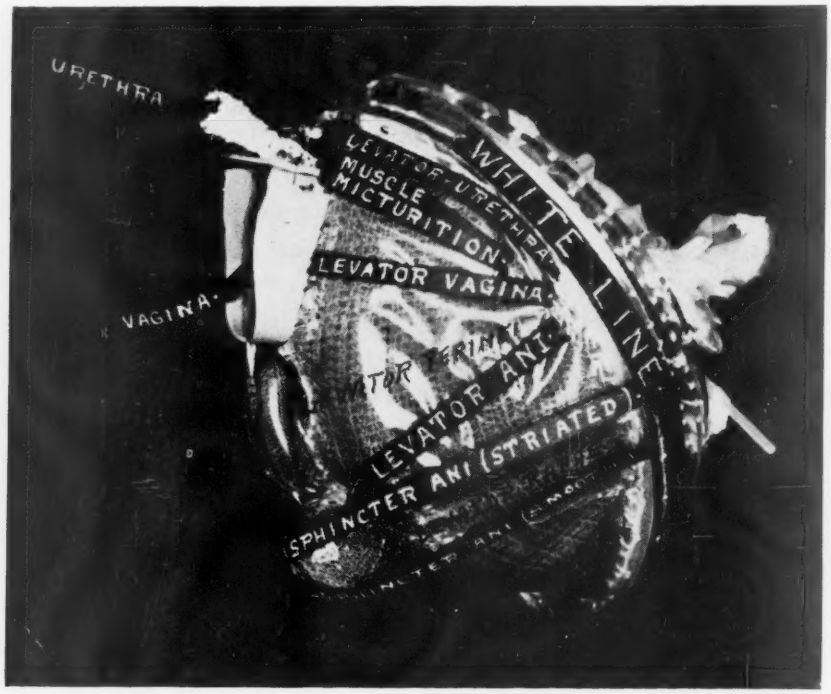


Fig. 1.—Shows the model with the layers closed. All five layers are in contact and can be opened. In the upper four layers, the muscle tissue is smooth, while in the lower or fifth layer all muscle tissue is striated.

*Layer 4.*—Comprises the rectum from the sacrococcygeal junction to where it passes through the sphincter ani externally. The rectum is held in an enveloping tensile sheath of fascia endopelvina which folds posteriorly to form its mesentery. Connective tissue arises from ischiococcygeal ligaments, passes to the rectum, gives it support, and keeps it in position.

*Layer 5.*—Comprises the levator muscle, which is wholly striated. The muscle can be divided into six component pairs of bands (one band from the left side meeting its corresponding band from the right side to move an organ in the sagittal plane of the pelvic floor). These bands in order, from front to back, move:

1. The vaginal wall under the urethra (Fig. 3)
2. The lateral walls of the vaginal orifice (Fig. 3)
3. The perineal body
4. The anus
5. The raphe
6. The coccyx.

Each component pair can function apart from another pair or in concert with it. The levator components have origin in the white line, are striated

muscle, have sheaths and have insertions into organs. They have a maximum length which is quite liberal and equal to the length of the sheath in extension. The insertions are loosely held together when away from the sphincter and are endowed with a great range of separation to prevent laceration when the fetus passes through the pelvic floor.

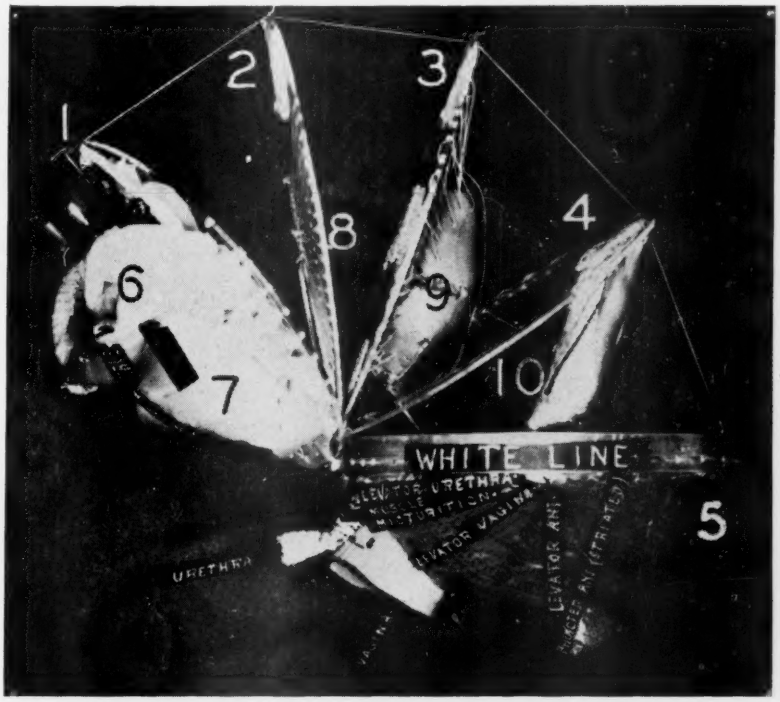


Fig. 2.—Shows the same model with the layers separated. As in the paper, the "white line" is the basic structure. Layers 1, 2, 3, and 4 are opened up, and layer 5 is shown below the "white line" in this illustration. The numbers designate:

1, 2, 3, 4, and 5. Layers
5. Levators muscles
6. Uterus
7. Bladder
8. Cervical supports
9. Vagina and supports
10. Rectum and supports.

The sphincter ani muscle bears the same relation to the levator ani muscle as the cuff to the sleeve of a shirt. The sphincter ani muscle, also striated, has two functions:

1. To pull together the insertions of all the levator components which make up the pelvic floor, and

2. To cut off voluntarily the evacuation of feces by compressing the sphincter ani internal (smooth muscle).

*The Vagina.*—Normally the collapsed walls are in contact and the cervix bears a certain relation to the line joining the heads of the femurs. A fully distended nulliparous vagina (Fig. 4) holds about 180 c.c. fluid (3 per cent sodium iodide). A piece of metal is placed in the external os of the cervix. X-rays are shown (superimposed) and indicate the position of the cervix: 1. in relaxation; 2. bearing down; 3. traction; 4. with vagina fully distended.

By distention, the cervix is transported about 2 inches toward the promontory of the sacrum. The lateral view shows where the bladder, the cul-de-sac, and the rectum lie. When radioactive elements are used to treat the cervix or uterus, and the vagina is distended with packing, damage may occur to the sigmoid, and even to the ileum.

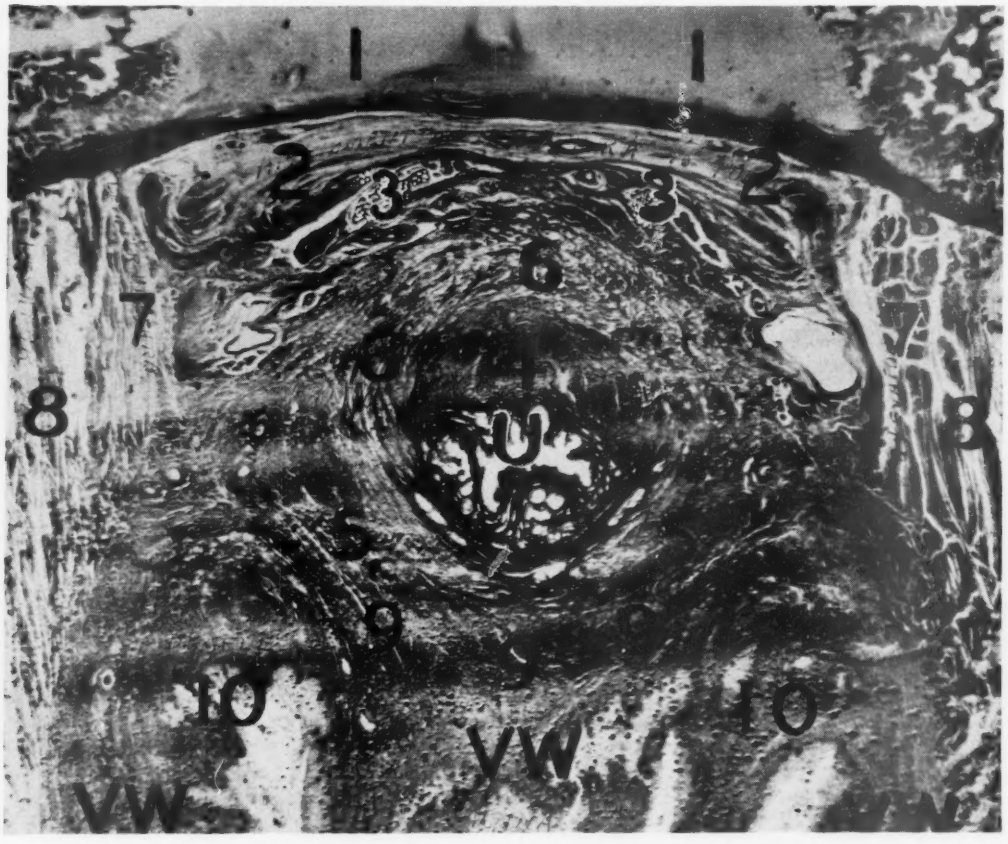


Fig. 3.—A histological section, cut at right angles to the axis of the urethra, showing the urethra, the levator muscles, the dimples, and the vaginal wall. The symphysis pubis is cartilagenous. The urethra is attached to it by connective tissue (its only fixed portion). The levator urethrae muscles with both origins and insertions are shown, as are similarly, the levator vaginae muscles. One sees how the dimple is formed. The anterior vaginal wall and the wall of the urethra are fused. A portion of the muscle of micturition appears, and from its thickness one can appreciate its strength. The letters and figures on the photograph designate:

U Urethra
VW Vaginal wall
1. Symphysis pubis (cartilagenous)
2. Attachment, urethra to symphysis
3. Urethral vessels (enter near attachment)
4. Circular smooth muscle, urethra } true sphincter
5. Longitudinal smooth muscle, urethra }
6. Part of the muscle of micturition (striated)
7. Levator urethrae muscle
8. Levator vaginal muscle
9. Fusion vagina and urethra
10. Dimple.

*Cleavage Planes.*—There are only two cleavage planes bordering on the vaginal wall (where the adjacent organs are held loosely to it by areolar connective tissue). One plane, the vesicovaginal, lies between the bladder and vagina

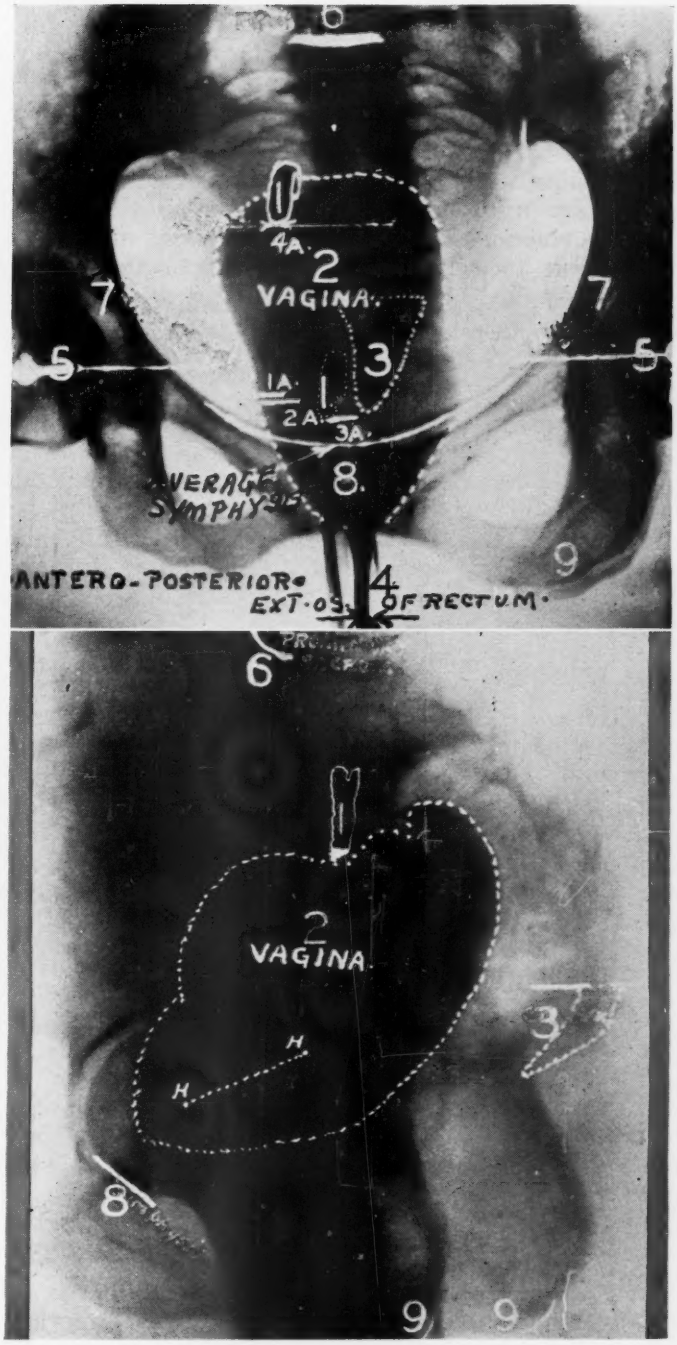


Fig. 4.—Shows the x-ray of a nulliparous vagina fully distended with 180 c.c. of a 3 per cent solution of sodium iodide. The anterior-posterior view appears above, the lateral view below.

1 A. Position of the external os of the cervix when the patient was relaxed.

2 A. Position of the cervix when bearing down.

3 A. Position of the cervix when under traction.

4 A. Position of the cervix when the vagina is distended.

Also shown are: 2. Vagina, 3. Coccyx, 4. Anus (external os of the rectum), 5. Heads of the femur, 6. Promontory of the sacrum, 7. Ischial spines, 8. Symphysis, 9. Tuberosity of the ischium.

and through it good supporting tissue to restore and repair the bladder and vagina can be reached, and the other plane, the rectovaginal, lies between the rectum and vagina, and through it good supporting tissue of vagina and rectum can be reached to repair and restore any of these organs displaced by labor injury.

*First Stage of Labor.*—The cervix commences to dilate, the cervical and vaginal supports loosen until the cervix and attached vagina reach the white line. The uterine contractions exert a pull on the cervix until the greatest plane of the fetal head passes the white line. If the first stage of labor is long, its length and intensity should be given as much consideration as the second stage. There are indications in current literature that, in labor, the uterine muscle is very active near the cornua, and that the cervix and lower uterine segment are comparatively passive.

*Second Stage of Labor.*—The second stage begins with the first pushing pain and marks the transfer of the pull of uterine contractions from the cervical rim to the attachment of the levator muscle to the vagina. If pudendal block analgesia has been selected, now is the time to give it, so that the levator muscles will not impede the passage of the head through the vaginal canal. Pudendal block seems to accelerate the descent of the occiput posterior head. Close observation should be kept to see that the anterior vaginal wall (with the bladder above) is pulled up over the head. If not, a Deaver retractor should be placed between the fetal head and the cervix, the vaginal wall, and the bladder and urethra.

As the head presses on the pelvic floor, the striated muscles stretch but have limited elongation, and, once this limit is reached, something has to give way for the head to pass. Here the prophylactic episiotomy (median) prevents: 1. Concealed damage to the levator muscle insertions moving the urethra and vaginal orifice; 2. concealed damage to the levator muscle insertions moving the perineum; 3. concealed damage to the inner margin of the sphincter ani muscles.

The author much prefers median episiotomy. He can find the incised fascia better and hence do a more satisfactory repair.

*Third Stage of Labor.*—This stage should not be rushed. If no interference has been used in the first stage and in the first half of the second stage, usually damage to the cervix is small and there is not much bleeding. If bleeding continues, all possible sources are explored. The cervix, sulcus tears (anterior, posterior, and lateral), and the episiotomy incision should be examined. Repairs of sulcus tears are done by approximating the full depth of the faces of the tears with interrupted No. 00 plain catgut sutures. The repair of the levator, the sphincter ani, and Colles' fascia are all accomplished by approximating the fascia only with continuous No. 00 plain catgut. Fig. 6 greatly clarifies our understanding of the rectum and one can learn from it the significant ideas necessary to a simple repair of a third-degree laceration.

*Post Partum.*—Normal examination is made on discharge. The patient is advised to urinate frequently in order that the uterus will get a chance to take the normal position. At four weeks post partum, the patient is again examined to determine the extent of involution of the cervix and uterus. At this time about 25 per cent of the patients have a markedly patulous cervical canal filled with mucus. The uterus is frequently retroverted and the patient's general condition seems below average. The mucus is removed from the cervix and the canal is packed with applicators saturated with Negatan or 10 per cent solution of silver nitrate. One week later, the patient is much better, the cervix almost closed, nearly free of mucus, and about 30 per cent of those who had postpartum

retroversion now have the uterus in place. This procedure has paid dividends in end results.

*Prolapse.*—The prolapse of the uterus and cervix only appears here. When a cervix is amputated, as in a Fothergill operation, prolapse is mostly relieved. Labor with poor involution of the uterus and cervix together with cervical infections contributes most frequently to prolapse. Prolapse of the cervix and uterus frequently drags down the kidneys and the ureters, and, after the uterus and cervix have been removed, and the prolapse corrected, the kidneys rise to an almost normal level (Fig. 5).

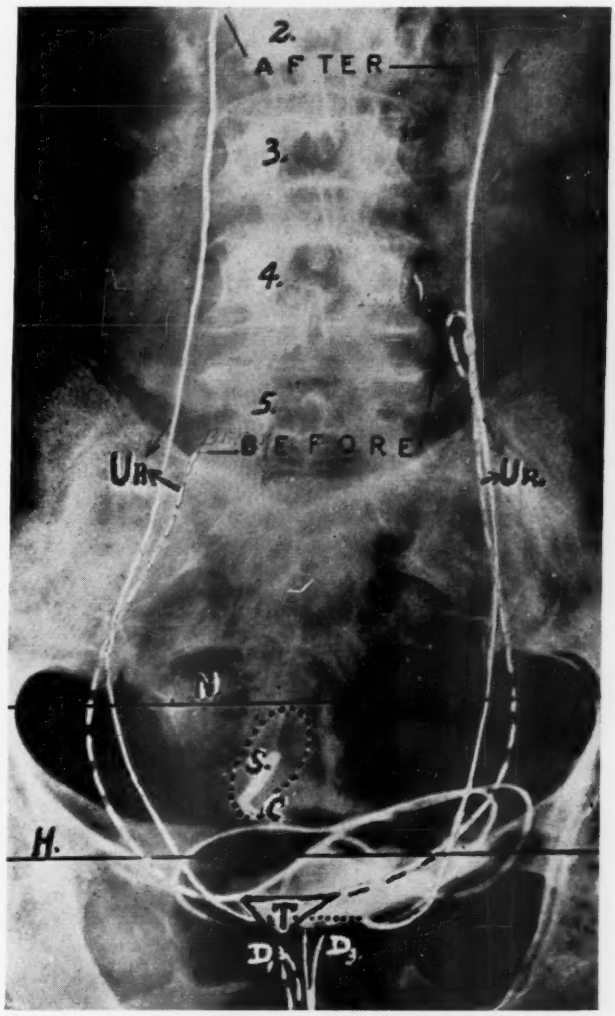


Fig. 5.—Shows one roentgenogram of the bladder, the ureters, and the replaced prolapsed uterus and cervix, superimposed on a second roentgenogram of the bladder, and ureters which was made after operation for prolapse (the cervix and uterus being removed).

S. Sound in uterus, one end attached to cervix, C.

*Before* indicates the level of the kidneys before operation and shows the extent of their prolapse.

*After* indicates their level after operation which is normal.

*Repairs.*—All damages to the cervix should be repaired immediately after delivery. If one sees a new patient who has a cervical laceration with a healthy cervical mucosa, extensively exposed to the vagina, the cervix should be repaired.

A uterus and cervix in prolapse after menopause should be removed and all accompanying plastic repair done. Great care should be taken to free the urethra of all adhesions and to pull the ends of the levator urethrae snugly under the urethra. Great care should be taken to repair a laceration of the

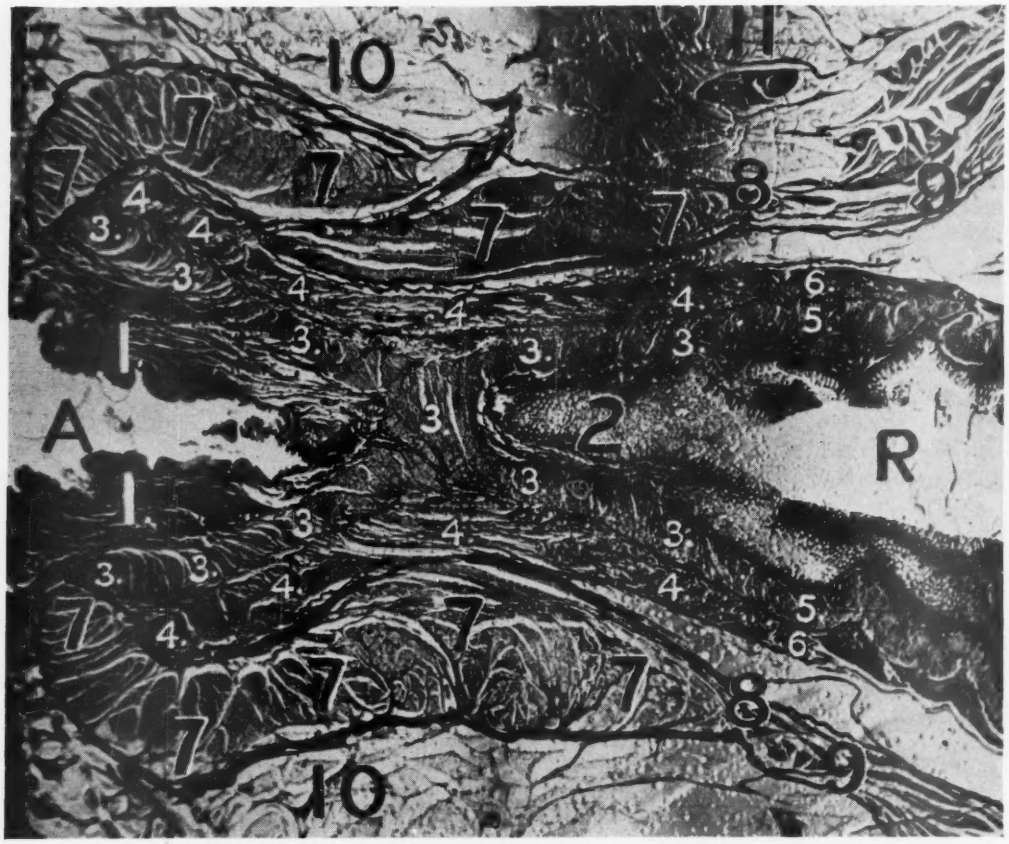


Fig. 6.—A histological section cut through the rectum, the plane being at right angles to the sagittal plane and through the axis of the sphincter ani. One can recognize the external sphincter ani muscle (striated) on either side of the canal, and its junction with the levator ani muscle. To consummate the ideal repair of a third-degree laceration, one must suture the opposite junctions together. The internal sphincter ani muscles (longitudinal and circular, smooth) are easily identified. Also shown are the pudendal vessels, the ischiorectal fossae, the rectal mucosa, the anus and the rectum. The letters and numbers on the photograph designate:

A Anus
R Rectum
1. Anal mucosa
2. Rectal mucosa
3. Circular anal muscle (smooth)
4. Longitudinal anal muscle (smooth)
3 and 4. Sphincter ani internal
5. Circular rectal muscle
6. Longitudinal rectal muscle
7. External sphincter ani (striated)
8. Junction sphincter and levator ani muscle
9. Levator ani muscle (striated)
10. Ischiorectal fossae
11. Pudendal vessels.

perineum by approximating the keypoints, junction of levator to sphincter ani muscles) and then approximating all other fascial layers with No. 00 plain catgut sutures (Fig. 6).

All muscular repairs can be perfectly accomplished when corresponding fascial edges are approximated. For ideal secondary repairs, these fascial edges must be denuded of scar tissue, visualized, and meticulously approximated to obtain a result possessing good function and minimum scar tissue.

## Comments and Conclusions

1. Undernutrition of every patient must be corrected first, if we expect to get optimum healing and commendable end results.

2. This gynecological and obstetrical study has been made to elucidate the relation of the genital organs and their supports to the white lines, the ischiococcygeal ligaments, and the coccyx. The structures have been divided into five layers. The upper four layers are composed of the genital organs, their muscles and connective tissue supports, all muscle tissue being smooth. The fifth, and lowest layer, is composed entirely of striated muscles.

3. In Layer 1, postpartum retroversion, an associated subinvolution of the uterus, or an indolent cervix, together with an infrequently emptied bladder in some patients, creates a problem. Treating the cervix from the fourth to the sixth week post partum and having the patient urinate on schedule will pay good dividends in end results.

4. Prolonged subinvolution of the cervix and uterus and infection of the cervix in time lead to lengthening of the cervical and vaginal supports; prolapse begins, falling of kidneys and bladder follow, and unrecognized or concealed labor damages appear, together with a train of unexpected symptoms.

5. Sulcus vaginal tears nearly always damage rectal supports and frequently injure some division of the levator muscles and contribute to a patient's misery.

6. *Labor:* The first stage duration should be accorded as much serious attention as the second stage. The first pushing pain is a critical time in labor. At this time (a) the fully dilated cervix is pulled up over the maximum plane of the fetal head; (b) the pull of the uterine contractions is transferred from the cervix to the levator muscles attached to the vaginal orifice; (c) the pudendal block, if this method of delivery has been selected, should be commenced; (d) forceps can now be applied with little damage to the cervix and lower uterine segment, but not necessarily to the vaginal canal supports; (e) prophylactic protection of the cervical rim, the anterior vaginal wall, and the urethra can profitably be carried out by placing a Deaver retractor between the cervix and the head and leaving it there until the head reaches the pelvic floor. Prophylactic conservation of the urethra, the vaginal orifice, and the levator muscles can be accomplished by the median episiotomy made sagittally through the perineal body to facilitate an easy delivery of the head.

7. Working familiarity with the two lines of cleavage will be a great asset in getting satisfactory results in all plastic repairs.

8. The vagina distends in the second stage of labor to have a diameter nearly three times the size of the distended nulliparous vagina.

9. When the uterus and cervix prolapse, the bladder, ureters and kidneys are all pulled down. When the prolapse is relieved, the kidneys return to their normal level.

10. The junction of the levator ani muscle and the sphincter ani muscle is a crucial point. When divided in episiotomy, they must be approximated after delivery to accomplish a creditable repair.

11. All repair of levator muscles, sphincter ani muscles, perinei muscles and Colles' fascia must be consummated by approximating their sheaths after episiotomy. In secondary repair, scar tissue must be removed.

12. Restoration of partially destroyed or displaced structures must be accomplished by attaching them to good supporting tissue coming from the white line and this restoration must be *maintained.*

The author wishes to express his appreciation to those members of the staff of the Woman's Hospital, who, by argument, suggestion, or discussion, have made this contribution possible.

930 Park Avenue

## Discussion

DR. WILLIAM F. MENGERT, Dallas, Tex.—My interest in the supportive function of the pelvic fascias began in 1933 following a prolonged discussion with a member of this Association concerning so simple a question as, "What holds the uterus in place?" Since we could not agree, I devised an experiment to test the question. If all the structures attached to the uterus are severed one by one in a fresh cadaver, during which process a constant downward traction is applied to the cervix, those structures contributing most to uterine support will manifest themselves. The experiment was conducted during the course of post-mortem examination on each of nine fresh female cadavers with anatomically normal genitals. It was clearly demonstrated that the tissues surrounding the cervix and the upper vagina supported *both* organs. In other words, not only paracervical, but also paravaginal tissues contribute to uterine support. The slight amount of support contributed by the sacrouterine "ligaments" stems from the fact that they are condensations of the paravaginal tissues. Actually, they are not true ligaments.

Especially noteworthy in the cadaver experiment was the total lack of support from the round ligaments and other structures attached to the region of the uterine fundus. When extensive second-degree prolapse was produced experimentally, the round ligaments hung in lax curves and were not drawn tight, despite the uterine displacement. Normally, the round ligaments are not uterine suspenders and do not function in maintenance of habitual ante- or retroversion. We know they are essentially muscle tissue, that they hypertrophy during pregnancy, contract with the uterus during labor, originate at the fundus, and insert in the vulva. Perhaps their sole function occurs during labor, to prevent the uterine fundus from "backing away" from the vulva.

Forty and more years ago, Tandler taught that the normal uterus is a movable organ. In 1936, Harris, Mengert, and Plass demonstrated with bimanual examination that it alters its position in response to postural change. The experiment was conducted on twenty young women with normal pelvic viscera, but confined to bed with pulmonary tuberculosis. Diddle, Mengert, and Earl in 1939 confirmed this response of the uterus to postural change by objective demonstration on normal women, and women with prolapse, by means of roentgenograms and superimposed photographs.

In the light of the foregoing, and of clinical experience, it is difficult for me to accept the belief that failure of involution produces an exhausted, below-par woman with a backache and partial prolapse. It is difficult for me to believe that subinvolution of the uterus is fre-

quently a forerunner of prolapse of the cervix. I do not think that it is necessary to empty the urinary bladder every three hours, or that retroversion will result if more than eight ounces of urine remain in the bladder for long periods of time. We have greatly simplified our puerperal care. Women are allowed to get out of bed to go to the bathroom as soon as they are conscious. In consequence, catheterization of the puerperal woman is virtually unknown. On the gynecologic ward, we pay no attention in the average patient to the concept of residual urine. Our routines include catheterization only for distress. These, and many other simplified measures, have been successfully applied on our wards to numbers of thousands of obstetric and gynecologic patients.

I do not think that lengthening of the round and uterosacral ligaments has anything to do with the occurrence of retroversion. I do not think that it is either necessary or desirable to protect the anterior vaginal wall with a Deaver retractor during the expulsive stage of labor.

Kantor, working at Parkland Hospital, recently studied the urinary bladder during labor by means of roentgenograms and indwelling rubber balloons attached to a pressure recording system. He established, beyond peradventure of doubt, that after the fetal head descends into the bony pelvis maximum pressure on the urinary bladder at the height of uterine contraction is but a few millimeters of water, and that our worries regarding potential danger to the urinary bladder during spontaneous labor are not well founded.

DR. HAROLD L. GAINEY, Kansas City, Mo.—The mandate in the title, "Know the Pelvis," is one, by the author, to himself, which he hopes will attract others. His detailed histologic studies on the muscle of micturition previously reported and this paper are testimonials to his sincerity and qualifications to do so.

In this discussion he has broadened the scope to include not only the concept of the pure anatomist but has included the dynamic aspects involved in the processes of pregnancy, parturition, and the puerperium. These less fixed phases are far more difficult to understand and interpret because of their complex variables. For example, the influence of ethnic characteristics demands that we use some restraint in our effort to control the end results of parturition by what may be ill-advised and damage-producing procedures. They should also temper our reports of accomplishments. The American Negro, although neglected by trained specialists in obstetrics, survives with less damage than the European races.

McKelvey states that the greatest number of prolapse cases is around Manchester, England, and that it is rare in China. Reis states that Jewish women have a high incidence, while Torpin, Findley, and others report a high incidence of spina bifida occulta in women with uterine prolapse. Within races there is evidence of genetically controlled variations similar to the almost 100 per cent family history of varicosities of the extremities.

The essayist states, "Many a woman is left with a retroversion she did not have before pregnancy because we obstetricians have neglected to help many of our postpartum patients finish up the involution of the cervix, uterus, and supports from four to six weeks after delivery. Consequently, she remains below par, has backache, and goes about exhausted for months, ending up with partial prolapse of the uterus and cervix some years later." Our impression is that the retroversion more likely is a "symptom" accompanying the other complaints and in many instances corrects itself spontaneously as observed, requiring at most the temporary use of the pessary only as a part of general hygienic measures. This we do, and have without proof the impression of benefit.

The procedure recommended at one month post partum, of removing the normal alkaline protective plug of mucus with application of irritating drugs making possible the invasion of ever present pathogens, to me is questionable. The physiologic changes, requiring 280 days of gestation, that make parturition a near normal physiologic process, are not reversible in a precipitous fashion. Eight weeks will accomplish this as a functional fact but not anatomically in a good per cent; twelve to sixteen weeks are required in some, depending on factors of general health, diet, and demands upon the body as a whole.

The next remark that aroused interest was, "Many a woman has had the levator support of her urethra torn and this predisposes to a relaxed urethra with incontinence." This observation we have recorded occurring in 5 per cent of primiparas and 28 per cent of multiparas. Of these, 16 per cent of the primiparas and 7.3 per cent of the multiparas had stress incontinence. Our studies have further suggested, not only because of damage in this area but because of the results noted throughout the vagina with cystocele, rectocele, and vaginal prolapse, that we give thought to the physiology of the second stage of labor and prevent or minimize the damage associated with it.

The first stage of labor is well respected by most, the second and third stages find many interfering with the normal mechanism. There is no more reason to doubt the efficiency of this physiologic mechanism than that of the first stage. I am sure there would be less damage if operative interference in the second stage were less radical and along a physiologic pattern.

The intrinsic weakness of the vaginal supporting structures follows a law of embryologic oncology that prevents any hollow viscus from developing a firm fascial sheath, thereby permiting normal functions of coitus and parturition. Hormonal influences and chronic passive congestion bring about enough softening to make parturition possible with a minimum of damage to this vulnerable area. Further, there is a uterovaginal mechanism in the second stage that cannot be denied its place as a protective factor to the vagina against the advancing fetus.

This uterovaginal mechanism is accomplished at complete dilatation by progressive shortening of the uterine musculature and cervical connective tissue fibers. This shortening, by drawing high out of the pelvis the external os with its attached vagina, gives counter pull against the advancing fetus. Our practice has been, when using outlet forceps, to apply them between contractions and exert traction only during the height of a contraction. At the early stages of perineal distention a mediolateral episiotomy is done to prevent further elongation of the vagina, damaging its attachments posteriorly to urogenital diaphragm and endopelvic fascia covering the levators and to prevent circumferential stretching that might injure the urogenital diaphragm and levator attachments anteriorly supporting the urethra.

We reviewed our statistical studies in an effort to arrive at an explanation for the acquisition of cystocele, rectocele, and detachment of the urethra. Multiparity was considered because of the increase over primiparous patients and two factors suggested themselves: one the precipitous nature of the second stage and the other the increase in the size of the baby. In the primiparous patients with detachment of the urethra the length of labor was longer, confirming the opinion of others that pressure and ischemia are factors.

# A REPORT ON THE CESAREAN SECTIONS DONE IN ST. VINCENT'S HOSPITAL, NEW YORK*

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*(From the Department of Obstetrics and Gynecology)*

BECAUSE of the increased prominence of this operation and the resultant widespread interest, a survey made of all the cases of cesarean section in one institution should provide some interesting data and conclusions.

This report includes all the cesarean sections, 536 in number, performed on the obstetrical service at St. Vincent's Hospital, New York, during the first fifteen years of the operation of this service, from 1932 to 1946, inclusive. It includes both private and ward cases. The total number of deliveries during this period was 15,429, and the incidence of cesarean section was 1:29. Of the total number of deliveries, 6,414 were private cases and 9,015 ward cases. The incidence of cesarean section was consistently higher in the private cases (1:17) than in the ward group (1:57). There were 297 low flap sections, an incidence of 55.4 per cent; 215 classical, 40.1 per cent; 16 extraperitoneal operations, 3 per cent; and 8 hysterectomies, Porro, 1.5 per cent. There were ten maternal deaths, all in the classical operation group, a mortality of 1.86 per cent of the total cesareans.

The operations were done by thirty-two different operators, twenty-five of whom were members of the attending staff and seven of the courtesy staff.

The incidence is shown in Table I. It is arranged so that the rate per hundred cases each year is given in the private and ward cases. There is a steady rise from 1.5 and 3.4 to 2.7 and 6.9, respectively.

The high incidence may be the result of judgment on the part of the obstetrician or the demands of the patients for the safety of their babies; nevertheless, with the high incidence we are always confronted with the possibility of a higher maternal mortality. The relationship between incidence and mortality in this series has not, however, been affected by the rapid rise in incidence.

There were more than twice as many cesareans performed on the private patients as on the ward patients. The main reason for the higher course of the upper curve in the table has been the arbitrary choice of cesarean section in the private case. Some obstetricians have deliberately chosen cesarean section in preference to the vaginal delivery in their debatable cases. No doubt anxiety about the private case has been the deciding factor in their choice. Some men trained in abdominal surgery, who do relatively few obstetrical cases, perform a cesarean as the easiest way out of a dilemma. Moreover, consultations do not always safeguard proper indications in some cases, as is so ably expressed by Hawks when he says "they [the consultants] are often merely politely agreeable."[1]

*Presented, by invitation, at the Fifty-Ninth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 9 to 11, 1948.

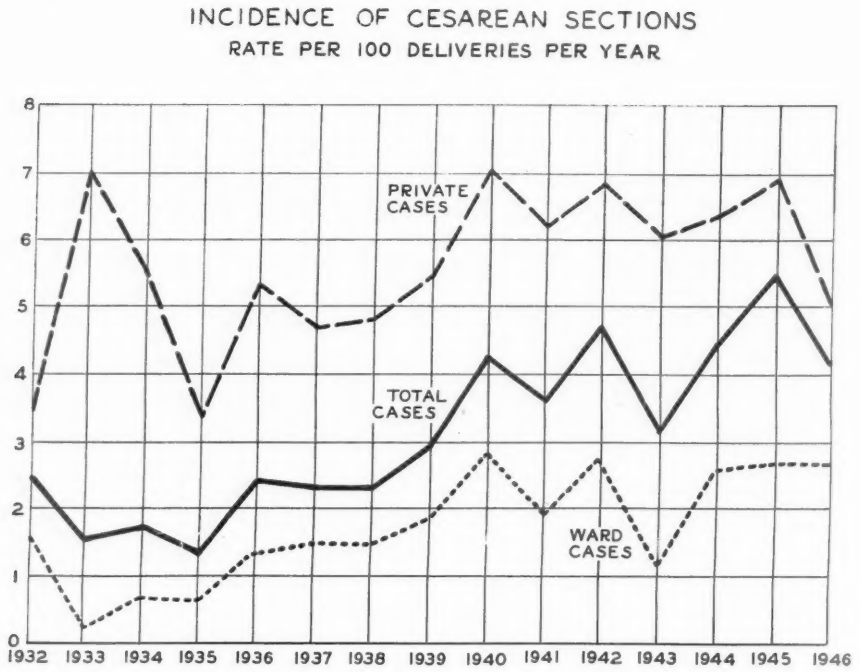


Fig. 1.

TABLE I

## INCIDENCE OF CESAREAN SECTIONS IN WARD AND PRIVATE CASES

| YEAR | TOTAL DELIVERIES | | | CESAREAN SECTIONS | | | INCIDENCE OF CESAREAN SECTIONS | | |
|---|---|---|---|---|---|---|---|---|---|
| | TOTAL | WARD | PRIVATE | TOTAL | WARD | PRIVATE | TOTAL | WARD | PRIVATE |
| 1932 | 121 | 63 | 58 | 3 | 1 | 2 | 1:40 | 1:63 | 1:29 |
| 1933 | 525 | 425 | 100 | 8 | 1 | 7 | 1:66 | 1:425 | 1:14 |
| 1934 | 750 | 588 | 162 | 13 | 4 | 9 | 1:58 | 1:147 | 1:18 |
| 1935 | 820 | 610 | 210 | 11 | 4 | 7 | 1:74 | 1:152 | 1:30 |
| 1936 | 739 | 532 | 207 | 18 | 7 | 11 | 1:41 | 1:76 | 1:19 |
| 1937 | 815 | 604 | 211 | 19 | 9 | 10 | 1:43 | 1:67 | 1:21 |
| 1938 | 934 | 685 | 249 | 22 | 10 | 12 | 1:42 | 1:68 | 1:21 |
| 1939 | 807 | 549 | 258 | 24 | 10 | 14 | 1:34 | 1:55 | 1:18 |
| 1940 | 870 | 572 | 298 | 37 | 16 | 21 | 1:24 | 1:36 | 1:14 |
| 1941 | 1,000 | 615 | 385 | 36 | 12 | 24 | 1:28 | 1:51 | 1:16 |
| 1942 | 1,251 | 654 | 597 | 59 | 18 | 41 | 1:21 | 1:36 | 1:14 |
| 1943 | 1,845 | 1,104 | 741 | 58 | 13 | 45 | 1:32 | 1:85 | 1:16 |
| 1944 | 1,647 | 826 | 821 | 73 | 21 | 52 | 1:22 | 1:39 | 1:16 |
| 1945 | 1,365 | 481 | 884 | 74 | 13 | 61 | 1:18 | 1:37 | 1:14 |
| 1946 | 1,940 | 707 | 1,233 | 81 | 19 | 62 | 1:24 | 1:37 | 1:20 |
| TOTAL | 15,429 | 9,015 | 6,414 | 536 | 158 | 378 | 1:29 | 1:57 | 1:17 |

## Indications

The various indications for the cesareans are listed in Table II. Many patients had several indications, and these are classified according to the major indication in each case.

TABLE II. CHIEF INDICATIONS FOR CESAREAN SECTION

| | |
|---|---|
| Contracted pelvis (all types) | 240 |
| Cephalopelvic disproportion | 82 |
| Placenta previa | 33 |
| Pre-eclamptic toxemia and nephritis | 29 |
| Previous cesarean section | 32 |
| Elderly primipara | 21 |
| Previous extensive plastic repair | 16 |
| Pelvic tumor (fibroids) | 12 |
| Pelvic tumor (ovarian cyst) | 1 |
| Cardiac disease | 7 |
| Diabetes | 8 |
| Unengaged breech | 8 |
| Large baby | 5 |
| Cervical dystocia | 6 |
| Transverse presentation | 4 |
| Rupture of uterus | 3 |
| Elective | 2 |
| Previous myomectomy | 2 |
| Premature separation of placenta | 3 |
| Twins (previous section) | 2 |
| No engagement (vertex) | 2 |
| Mental depression | 2 |
| Fetal distress | 2 |
| Threatened rupture of uterus | 1 |
| Pulmonary tuberculosis | 1 |
| Previous complete laceration (2) | 1 |
| Osteoarthritis | 1 |
| Previous section, sterilization, implantation of tubes | 1 |
| Torsion of uterus | 1 |
| Midplane arrest | 1 |
| Prolonged labor | 1 |
| Face pesentation | 1 |
| Brain tumor | 1 |
| Sacroiliac injury | 1 |
| Psychopathic fear of labor | 1 |
| Carcinoma of rectum | 1 |
| Congenital dislocation of hips (arthroplasty) | 1 |
| Total | 536 |

The success of cesarean section has carried with it an inordinate broadening of the indications, so that many physicians feel that it is too frequently performed.

In 1918, the indications were very few; approximately 95 per cent were performed for some type of contracted pelvis. Since then, additional indications include almost every possible complication to which pregnant women are subject. Also, at that time, it was difficult to persuade the patient and her family to permit a necessary cesarean section. Today, if the labor seems too prolonged, the family and relatives ask why cesarean is not being considered or done. If the child should die by delivery *per vias naturales,* the implication in some instances is that the case has been mismanaged, that the physician should have known enough to do a cesarean section in the first place, and that if some other doctor (sometimes mentioned by name) had had the case he would have done a cesarean. I have encountered acquiescence to this at-

titude in certain members of the professsion. What has brought it about? No doubt the many reports of large series of cases with almost no mortality and the failure to study the reports properly. Also, I doubt that all men publish all their poor results, since we have been able to find so many casualties in the reports of the Maternal Mortality Committee of New York City.

What are the indications for doing a cesarean section? The absolute indications for cesarean section are few. The main one is the presence of pelvic deformity or contraction of such degree that the birth of a living child is absolutely impossible. Almost all other indications must be considered as relative, since it would be possible to deliver the fetus through the birth canal, though at the risk of a terrific sacrifice in fetal life and resultant damage and subsequent permanent invalidism to the mother.

What can we consider as relative indications? The most common is relative disproportion between the size of the fetus and the pelvic capacity. The severe degrees of contraction are easily recognized. The minor ones, the borderline types constituting the largest group, are more common and the ones with which we have to deal most frequently. The management of the borderline pelvic indications for cesarean continues to be a problem. There is always great danger in delaying the operation until there is exhaustion in the mother, which may lead to infection and other complications, perhaps even to the death of the child, irrespective of the type of delivery. In our series, there were 240 cases of contracted pelves of all types (44.77 per cent) and 82 cases of cephalopelvic disproportion (15.29 per cent), making a total of 322 cases. Of this number, 125 (38.82 per cent) had had x-ray and pelvimetry before operation.

Where real doubt exists, x-ray studies should be made early in labor, and interpretation should be made by both the obstetrician and the roentgenologist; otherwise, the report loses much of its value. The roentgenologist sees only one side of the picture and is not able to give a full, satisfactory report; he does not take into consideration the molding of the head, nor does he know the physical setup or make-up of the patient. Several of our babies were delivered through borderline pelves when the x-ray had reported a definite disproportion.

We often hear the question, "Shall we allow a test of labor?" What constitutes a test of labor? No two definitions are alike. I quite agree with Waters when he states that a "test of labor" depends upon the character, frequency, and effectiveness of first stage uterine contractions and correlated factors, such as physical status and emotional balance of the patient.[2] In our series, we found that the incidence of sections increased when there was a trial or test of labor and x-ray studies.

Previous operations, including cesareans, are also relative indications. In our series, 16 cases had had extensive vaginal plastic operations for partial prolapse, complete lacerations of the perineum, and rectovaginal fistula. Previous sections had been done in 143 cases. There were 107 with one previous section, 29 with two previous sections, four with three previous sections, one with four previous sections, and two with five.

Previous cesarean occurred as a major indication thirty-two times. Its indication is not always valid, for much depends on the type previously performed, the postoperative course, and whether it was done for an absolute or a relative indication. Previously sectioned patients bring up the question of whether we should subscribe to the doctrine of "once a section, always a section." I have in a few instances successfully delivered patients through

the pelvis who had had previous section for only relative indications. But one never knows how strong the uterine scar is, so that no matter how uneventful the convalescence may have been, I believe that it is not wise to wait and wonder if and when the uterus may rupture. Even though a patient has had pelvic deliveries after a section, it does not necessarily follow that she will go through another pregnancy safely. In most cases of a previous classical section, if the scar is thin, we do a repeat section about a week before the estimated date of confinement. Most of the reported ruptures have been through classical scars. According to Kerr[3] and Audebert[4] the percentage varies from 4 to 6 per cent. The generally accepted figure seems to be 4 per cent. Gepfert[5] reported a case of antepartum rupture of the uterine scar following low-flap cesarean section. With the potential rupture always in mind, it would seem that the best interests of the patient are served if she is carefully watched; and unless the head is well down and the cervix well attenuated, a cesarean should be done.

Other relative indications are the presence of fibroids and breech presentations. In twelve cases, cesareans were done because of fibroids. These were cases in which the fibroid was low down in front of the head, preventing its coming into the pelvis. Fibroids in other locations are no indication for cesarean. Eight cesareans were done for breech presentations. These were cases of early rupture of the membranes, short labor, closed cervix, and a large baby. Breech presentation per se is not an indication for section; instead, we should try to determine the true cause for the indication, whether it be a fetopelvic disproportion or some other complicating factor.

TABLE III. OBSTETRIC HISTORY OF PATIENTS

| | NO. OF CASES | MATERNAL DEATHS | | INFANT DEATHS | | STILLBIRTHS | | TOTAL FETAL MORTALITY | |
|---|---|---|---|---|---|---|---|---|---|
| | | NO. | RATE | NO. | RATE | NO. | RATE | NO. | RATE |
| Total | 536 | 10 | 1.86 | 27 | 5.04 | 25 | 4.66 | 52 | 9.70 |
| Primiparas | 311 | 6 | 1.92 | 16 | 5.14 | 16 | 5.14 | 32 | 1.028 |
| Multiparas | 225 | 4 | 1.77 | 11 | 4.88 | 8 | 3.56 | 19 | 8.44 |
| *Previous Sections:* | 143 | 2 | 1.39 | 5 | 3.49 | 0 | 0.00 | 5 | 3.49 |
| One previous section | 107 | 1 | 0.93 | 7 | 6.54 | 0 | 0.00 | 7 | 6.54 |
| Two previous sections | 29 | 1 | 3.44 | 1 | 3.44 | 0 | 0.00 | 1 | 3.44 |
| Three previous sections | 4 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| Four previous sections | 1 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| Five previous sections | 2 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |

Table III gives a résumé of the obstetric history of the patients. The mortality rate of 1.86 compares favorably with the general mortality rate of 2.51. The majority of these cases had elective cesarean section without trial labor. Two of the deaths occurred in patients who had had previous sections (one having had one, and the other having had two).

One hundred eleven of these cases had had previous vaginal delivery. Two of these mothers died following cesarean. There were twenty-four stillbirths and seven babies dying following delivery, a total fetal mortality of 31, or 8.52 per cent. Included in the number of stillbirths in these one hundred eleven cases were two sets of premature macerated twins and four full-term macerated babies.

Table IV gives the ages of patients. The most favorable age group seemed to be that in the twenties. In the small group of patients 38 years of age and over, the maternal mortality rate, as well as the fetal mortality rate, was more than doubled. This study would indicate that the risk to both mother and baby is markedly increased as the mother reaches the fortieth year group.

TABLE IV. AGE OF PATIENTS

| | ALL CASES | | | PRIMIPARAS | | | MULTIPARAS | | |
|---|---|---|---|---|---|---|---|---|---|
| | NO. OF CASES | MATERNAL DEATHS | | NO. OF CASES | MATERNAL DEATHS | | NO. OF CASES | MATERNAL DEATHS | |
| | | NO. | RATE | | NO. | RATE | | NO. | RATE |
| All ages | 536 | 10 | 1.86 | 311 | 6 | 1.93 | 225 | 4 | 1.77 |
| 13 to 19 years | 14 | 0 | 0.00 | 13 | 0 | 0.00 | 1 | 0 | 0.00 |
| 20 to 24 years | 83 | 0 | 0.00 | 61 | 0 | 0.00 | 22 | 0 | 0.00 |
| 25 to 29 years | 129 | 2 | 1.55 | 76 | 1 | 1.31 | 53 | 1 | 1.88 |
| 30 to 34 years | 135 | 3 | 2.22 | 68 | 2 | 2.94 | 67 | 1 | 1.46 |
| 35 to 39 years | 120 | 4 | 3.33 | 61 | 3 | 4.91 | 59 | 1 | 1.69 |
| 40 to 46 years | 54 | 1 | 1.85 | 32 | 0 | 0.00 | 22 | 1 | 4.52 |
| 47 years | 1 | 0 | 0.00 | 0 | 0 | 0.00 | 1 | 0 | 0.00 |

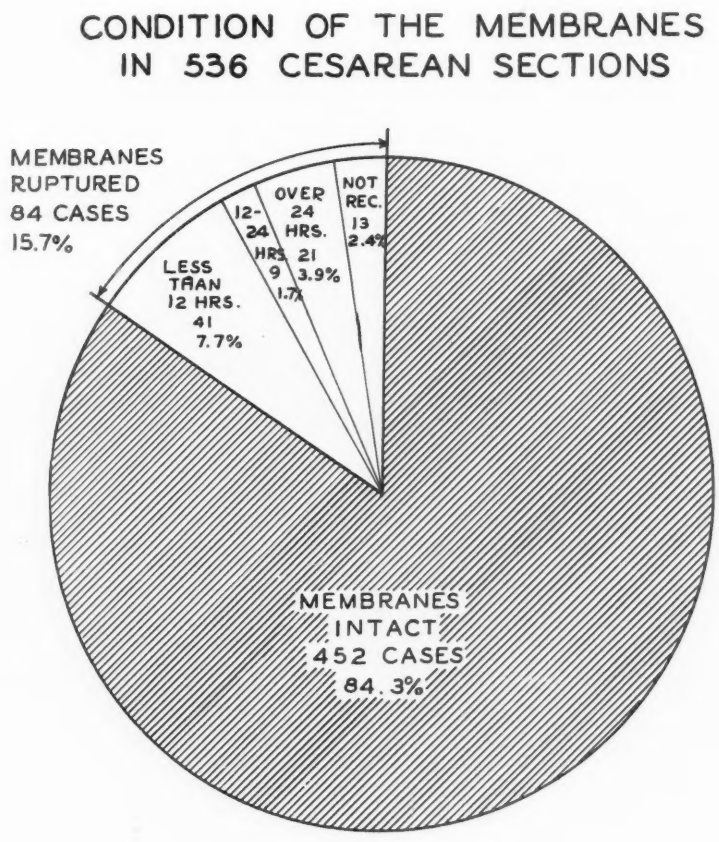


Fig. 2.

Table V shows the condition of the membranes. In women with intact membranes at the time of operation the maternal death rate is usually lower that in those in whom the membranes are ruptured. In contrast to this, our series showed the death rate was higher in the cases with intact membranes, nine cases, or 1.99 per cent.

TABLE V. CONDITION OF THE MEMBRANES

| | NUMBER OF CASES | MORBIDITY | | MORTALITY | |
|---|---|---|---|---|---|
| | | NO. | RATE | NO. | RATE |
| All cases | 536 | 66 | 1.23 | 10 | 1.86 |
| Membranes intact | 452 | 47 | 1.40 | 9 | 1.99 |
| Membranes ruptured less than 12 hours | 41 | 8 | 1.95 | 0 | 0.00 |
| Membranes ruptured 12 to 24 hours | 9 | 1 | 1.11 | 0 | 0.00 |
| Membranes ruptured 24 hours and over | 21 | 8 | 3.80 | 0 | 0.00 |
| Time of rupture not recorded | 13 | 2 | 1.54 | 1 | 0.77 |

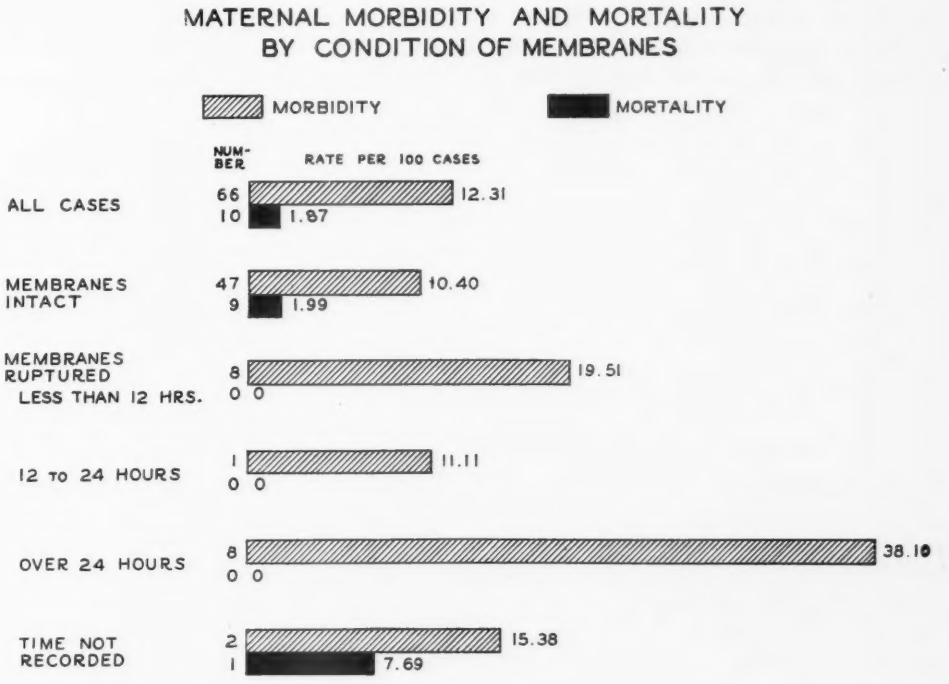


Fig. 3.

Table VI summarizes the maternal and fetal mortality in relation to the duration of labor before cesarean section was performed. It has long been recognized that the death rate is higher in those women having cesarean section the longer they have been in labor than it is in those sectioned prior to the onset of labor.

TABLE VI. DURATION OF LABOR

| | NO. OF CASES | MATERNAL DEATHS | | INFANT DEATHS | | STILLBIRTHS | | TOTAL FETAL MORTALITY | |
|---|---|---|---|---|---|---|---|---|---|
| | | NO. | RATE | NO. | RATE | NO. | RATE | NO. | RATE |
| All cases | 536 | 10 | 1.86 | 27 | 5.04 | 25 | 4.66 | 52 | 9.70 |
| No labor | 356 | 4 | 1.12 | 20 | 5.62 | 12 | 3.37 | 32 | 8.99 |
| Less than 6 hours | 30 | 1 | 3.33 | 0 | 0.00 | 3 | 10.00 | 3 | 10.00 |
| 6 to 12 hours inclusive | 54 | 4 | 7.4 | 3 | 5.55 | 2 | 3.70 | 5 | 9.25 |
| 13 to 24 hours inclusive | 51 | 1 | 1.96 | 2 | 3.92 | 5 | 9.80 | 7 | 13.72 |
| Over 24 hours* | 44 | 0 | 0.00 | 2 | 4.54 | 3 | 6.81 | 5 | 11.36 |
| Time not recorded | 1 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |

*Longest time of labor recorded was 84 hours. There were eight cases ranging from 62 to 84 hours.

Four of these maternal deaths occurred without labor, in patients with serious prenatal complications, such as pulmonary tuberculosis, severe grade of cardiac disease, toxemia, and brain tumor. If we were to omit these cases having severe prenatal complications, the elective group would show a low death rate, 1.1 per cent. In the group having section after from six to twenty-four hours of labor, there was a rise in maternal mortality. It is interesting to note, however, that there were no maternal deaths in the forty-five cases who had twenty-four hours or more of labor.

Table VII details the anesthesia used. Nearly all the cesarean sections were done with inhalation anesthesia, usually cyclopropane combinations, or gas-oxygen-ether combinations. There were only three cases of spinal anesthesia. Gas-oxygen-ether had the highest maternal mortality. Local anesthesia with inhalants was used in 13 cases.

TABLE VII. ANESTHESIA

| | NO. OF CASES | MATERNAL DEATHS | |
|---|---|---|---|
| | | NO. | RATE |
| Total | 536 | 10 | 1.86 |
| Cyclopropane-oxygen | 189 | 1 | 0.53 |
| Cyclopropane-oxygen-ether | 165 | 0 | 0.00 |
| Gas-oxygen-ether | 162 | 8 | 4.94 |
| Local with inhalants | 13 | 1 | 7.69 |
| Ether | 3 | 0 | 0.00 |
| Spinal | 3 | 0 | 0.00 |
| Gas-oxygen-ethylene | 1 | 0 | 0.00 |

## Choice of Type of Operation

Each operation has its place. The classical operation is the oldest and now the least often performed. It was the operation chosen by the occasional operator because it has always been the easiest to perform; yet, of all types of cesareans, it no doubt carries the highest percentage of postoperative deaths.

In our series, the pendulum has swung markedly from the classical to the low segment transperitoneal operation. We found the low segment operation the best for clean cases and the low transverse cervical incision the technique most suitable. The results shown indicate its superiority over the old classical and the reasons why it has so rapidly come to the front. Its use is one of the greatest single factors in reducing mortality in cesarean section. Also, another great advantage of the low segment operation lies in the fact that, because it is easy to demonstrate the anatomy and have full vision of the field at all times, this method can, without difficulty, be taught the members of the resident staff.

Fig. 4 shows the increase of the low cesarean section over the classical during the last seven-year period in our series. In many clinics, classical cesarean carries approximately a 5 per cent mortality; whereas the lower segment operation has only 1 or 2 per cent. That, of course, is another reason why the latter technique is rapidly replacing the classical. The classical operation is reserved for the elective case, i.e., the woman not in labor. It is very useful when speed is essential, as in cases of accidental hemorrhage with almost no dilatation and with mother and baby in danger. It may be the easiest operation in a cardiac case or the choice in a clean case of placenta previa.

Heretofore, the other types of operation were used in potentially infected cases; nowadays they are also done in the clean and elective cases. Thus the low flap is done in all cases, in early or late labor, with little or no contamination.

In our series, the Waters and Latzko operations, which have the advantage of allowing drainage, were done in the cases long in labor, potentially contaminated. There were sixteen such cases, among them eight which ranged from sixty-two to eighty-four hours in labor and in which both mothers and babies were saved.

The Porro operation is the choice for the badly contaminated case with a noncontractile, grossly infected uterus and for cases of Couvelaire uterus. In our series, it was done for nonremovable tumors in eight cases.

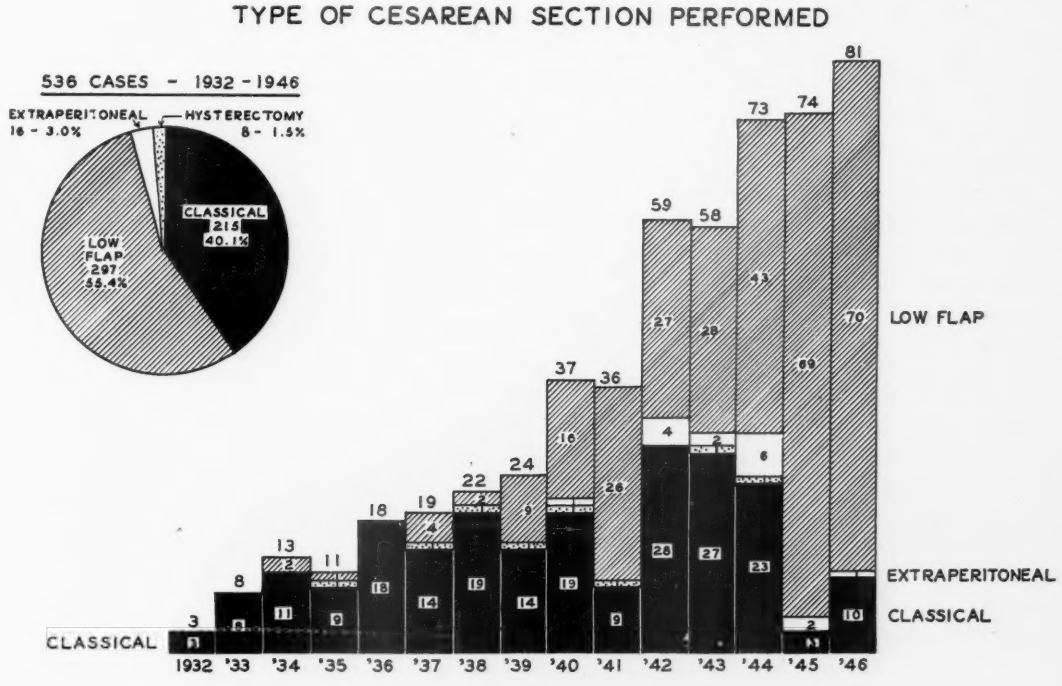


Fig. 4.

## Hemorrhage

In the antepartum period, we have to deal with two conditions: placenta previa, and partial separation of a normally implanted placenta.

A placenta removed from the lower uterine segment before it is dilated and attenuated by the passing child is not, as experience has shown, attended by serious hemorrhage; but the detachment of a placenta previa, following (or preceding) the delivery of a child *per vias naturales,* is always attended with great loss of blood, and many of these patients have died of postpartum hemorrhage for lack of sufficient contraction in the overstretched lower segment of the uterus.

In the treatment of placenta previa, cesarean section has come into greater prominence since Bill,[6] in 1927, reported the results of prophylactic blood transfusions and section. The Voorhees bag is sometimes mentioned; but unless one is experienced in the inserting of the bag, there is danger of increasing the separation and prolonging the labor. A few parous patients with a well-dilated, effaced cervix have been delivered safely vaginally. If the bag can be inserted without difficulty in the well-selected case, I feel that

it is a safe procedure. After delivery, whether from above or below, the uterus should be packed.

It is generally agreed that cesarean section is the method of choice in cases of placenta previa in the primipara; and also generally in cases of placenta previa when the cervix is undilated, when the fetus is at term, alive and viable, when there has been no vaginal interference, and when manipulation from below would be dangerous. The low cervical cesarean is the best type of operation for complete placenta previa, for other types presenting a closed cervix, and for the incomplete varieties of placenta previa when the cervix is long and undilated.

In our series, we had 33 cases (6.1 per cent) of placenta previa, with one death, which we charted as a preventable death, occurring in a para iii who had had two previous sections and who entered the hospital seven hours after the onset of bleeding.

Cases of partial separation of the placenta should be individualized, for the pathology varies from almost nothing to the very dangerous type known as uteroplacental apoplexy. In cases of partial separation in which there is only moderate hemorrhage and the fetus is viable, the decision of whether to do a cesarean section or to deliver from below is a difficult one. Mild forms of separation respond well to the usual therapy, especially in a multipara with a dilated and well-effaced cervix, a fetus of normal size, and a pelvis not too contracted. If the patient is in labor she will require careful observation; if the separation is accompanied by progressive symptoms of blood loss and shock, irregularity of the fetal heart, colicky pains, hard uterus, a cervix long and closed or rigid, a section should be done at once with plenty of blood replacement and shock therapy.

TABLE VIII. CAUSES OF POSTPARTUM MORBIDITY

| | | |
|---|---|---|
| Postpartum morbidity, all causes | 66 | |
| Sapremia | 21 | |
| Infected abdominal wound | 13 | |
| Pyelitis | 5 | |
| Pyelonephritis | 2 | |
| Pneumonia | 2 | |
| Phlebitis | 2 | |
| Shock | 2 | |
| Hematoma of wound | 2 | |
| Bronchitis | 2 | |
| Mastitis | 1 | |
| Tonsillitis | 1 | |
| Septicemia | 1 | |
| Parotitis (bilateral) | 1 | |
| Peritonitis (general) | 1 | |
| Cystitis | 1 | |
| Atelectasis | 1 | |
| Salpingitis | 1 | |
| Hemorrhage | 1 | |
| Postpartum convulsions | 1 | |
| Thrombophlebitis | 1 | |
| Secondary anemia | 1 | |
| Coryza and pharyngitis | 1 | |
| Heart conditions | 1 | |
| Suture of packing to uterus | 1 | |
| Total | 66 | Rate 12.3% |

In every cesarean section there is danger of hemorrhage, from the time the incision is made into the uterus until after the patient's return to her bed. The control of hemorrhage during operation upon a normal uterus would

seem to be a simple problem; yet, three women died after classical sections, two on the operating table, and one in bed seven hours following the section. The two deaths on the table were from separation of the suture line and hemorrhage, as confirmed by autopsy.

Still we have come a long way since 1905, when Dr. Rudolph Holmes[7] summed up the mortality in cesarean section by stating that cesarean section lowered infant mortality 30 per cent, but increased maternal mortality nearly threefold. Today, with our improved operative technique, adequate preoperative replacement of the blood lost, the control of hemorrhagic shock, cesarean section appears to be three times safer for the mother than is the expectant obstetrical treatment; this safety also holds true for the baby.

Table VIII lists the major causes of postpartum morbidity. The accepted morbidity standard in this series has been that any woman showing a temperature of 100.4° F. on any two successive days after the first forty-eight hours is considered morbid from childbirth. All wound complications, serious or otherwise, were included. Sapremia was our main cause of morbidity, 31.8 per cent; the next was wound complications of all kinds, 19.7 per cent.

TABLE IX

## CAUSES OF FETAL MORTALITY

### IN 215 CLASSICAL CESAREANS

| STILLBIRTHS | 9 | NEONATAL DEATHS | 14 |
|---|---|---|---|
| ABRUPTIO PLACENTAE | 3 | PREMATURITY | 5 |
| UNEXPLAINED | 2 | UNEXPLAINED | 4 |
| CARDIO-VASCULAR DISEASE (MAC.) | 1 | ATELECTASIS (PM.) | 2 |
| DIABETES (MAC.) | 1 | CONGENITAL HEART | 1 |
| TORSION OF UTERUS | 1 | LOBAR PNEUMONIA | 1 |
| CONGENITAL HEART (PM.) | 1 | HEMORRHAGE | 1 |

### IN 297 LOW FLAP CESAREANS

| STILLBIRTHS | 14 | NEONATAL DEATHS | 13 |
|---|---|---|---|
| LARGE BABIES (2) | | ATELECTASIS (PM.) | 4 |
| (1) 11 LB. 12 OZ. (MAC), UNEXPLAINED | 1 | HEMORRHAGE IN MEDULLA (PM.) | 2 |
| (2) 10 LB. 3 OZ., 24 HOUR LABOR | 1 | PREMATURITY | 2 |
| MACERATED | 3 | TOXEMIA | 1 |
| TWINS | 3 | RUPTURE OF LUNG | 1 |
| ASPHYXIA | 2 | HYDROCEPHALUS | 1 |
| ABRUPTIO PLACENTAE | 1 | MEGALOCEPHALIC | 1 |
| PREMATURITY | 1 | CONGENITAL ATRESIA OF SMALL INTESTINE (PM.) | 1 |
| UNEXPLAINED | 1 | | |
| ERYTHROBLASTOSIS | 1 | | |

### IN 8 HYSTERECTOMIES

| STILLBIRTHS | 2 |
|---|---|
| RUPTURE OF UTERUS (FETUS IN ABDOMEN) MACERATED | 1 |
| RUPTURE OF UTERUS, PLACENTA ACCRETA, FIBROIDS | 1 |

NOTE: THERE WERE NO STILLBIRTHS OR NEONATAL DEATHS FOLLOWING 16 EXTRAPERITONEAL SECTIONS.

Table IX shows the incidence of stillbirths found in classical cesarean section, 4.18 per cent; in low cervical section, 4.71 per cent. In the Porro group, the stillbirths were 25 per cent. There were no stillbirths and no neonatal deaths in extraperitoneal sections. The total fetal mortality in classical cesareans was 10.69 per cent. The total fetal mortality in low cervical sections was 9.99 per cent.

## Analysis of Maternal Deaths

In analyzing the ten deaths, we find that four of the patients died from causes complicating pregnancy and labor or from other systemic conditions, and that the method of delivery could not have been a factor in the cause of death. Six of the deaths occurred in the first six years of the service, after which there was one a year for the next four years. There were no deaths following cesarean section in the years 1937, 1938, 1940, 1941, 1944, 1945, and 1946.

TABLE X

MATERNAL MORTALITY

| | YEAR | AGE | PARA | STAT. | WEEKS PREG. | PAST HISTORY | ANTEPARTUM & INTRAPARTUM HISTORY | HOURS OF LABOR | POSTPARTUM HISTORY EXPIRED | POSTPARTUM HISTORY CAUSE | BABY | REMARKS | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1933 | 38 | I | P | 38 | NEGATIVE | NEPHRITIC TOXEMIA | 0 | AFTER 6½ HRS. | SHOCK | LIVING (4 LB. 7½ OZ.) | — | NON-PREV. |
| | 1933 | 32 | II | P | 39 | PULMONARY TBC. PREV. SECTION | PULMONARY TBC. ARR. PREV. SECTION | 0 | IN 24 HRS. | SHOCK | LIVING (7 LB. 9 OZ.) | — | NON-PREV. |
| | 1934 | 26 | I | P | 38 | NEGATIVE | GEN CONTR PELVIS | 9 | ON 4TH DAY | AC. INTEST. OBST. PERITONITIS | LIVING (6 LB. 8 OZ.) | COLOSTOMY | — |
| | 1935 | 34 | I | P | 32 | RHEUMATIC HEART DISEASE | CLASS II CARDIAC | 0 | AFTER 15 HRS. | CARDIO-VASCULAR COLLAPSE | EXPIRED IN 14 HRS. (2 LB. 9 OZ.) | — | NON-PREV. |
| | 1935 | 32 | I | P | 38 | NEGATIVE | GEN. CONTR. PELVIS ANDROID | 8½ | ON 7TH DAY | PERITONITIS | LIVING (6 LB 1 OZ.) | AC. ENDOCARDITIS AC. PERITONITIS † | NON-PREV. |
| | 1935 | 39 | I | P | 40 | NEGATIVE | CONTR. PELVIS C. P. D. | 4 | IN 7 HRS. | HEMORRHAGE | LIVING (8 LB. 10 OZ.) | SEPARATION OF UTERINE WOUND † | PREV. |
| | 1936 | 37 | I | W | 40 | NEGATIVE | LARGE BREECH | 24 | ON OPER. TABLE | HEMORRHAGE | LIVING (9 LB. 10 OZ.) | SEPARATION OF UTERINE WOUND † | PREV. |
| C | 1939 | 37 | VI | P | 42 | IST ECLAMPSIA 3 DIFF. INST DEL. | C. P. D. FAILURE TO ENGAGE | 6 | ON 4TH DAY | PERITONITIS | LIVING (8 LB. 10 OZ.) | — | NON-PREV. |
| | 1942 | 43 | III | P | 38 | 2 PREV. SECTIONS | PLACENTA PREVIA COMPLETE | 8½ | ON OPER. TABLE | HEMORRHAGE | EXPIRED IN 1/2 HR. (6 LB. 11 OZ.) | ADMITTED TO HOSP. 7 HRS. AFTER ONSET OF BLEEDING | PREV. |
| D | 1943 | 28 | III | P | 32 | 2 VAG. DEL. 1 MISCARRIAGE | BRAIN TUMOR | 0 | IN 32 HRS. | GLIOMA | TWINS LIVED 2 HRS. (PREM.) | GLIOMA OF LEFT LOBE † | NON-PREV. |

NOTE: ALL CLASSICAL CESAREAN SECTIONS. G-O-E ANESTHESIA EXCEPT FOR (C) CYCLOPROPANE AND (D) LOCAL.

NOTE: † INDICATES POSTMORTEM. UNLESS SO NOTED THERE WAS NO POSTMORTEM.

As the incidence of cesarean section markedly increased, there was a decrease in the maternal death rate. This decrease no doubt was brought about because of the holding of early consultations, the performing of cesarean sections earlier in labor, and the avoiding of prolonged labor with its various complications, among them maternal exhaustion and ruptured membranes.

Some of the deaths, those from hemorrhage, could have been prevented had we had then, as we have today, the improved operative technique, the adequate preoperative replacement of the blood lost, and the control of hemorrhagic shock. Today, thanks to a well-functioning blood bank for which donors are always available, we are able to give transfusions to patients whose hemoglobin and red blood counts are low. In our cases of hemorrhage, placenta previa, and premature separation of the placenta, blood is given before, during, and after the operation, if necessary.

## Résumé

In considering the 536 cesarean sections done at St. Vincent's Hospital by numerous obstetricians during the past fifteen years, we have made a sharp distinction between the ward and private cases. By contrast and comparison of these two services, we are able to render a more detailed report. This series shows that in the 536 cases (158 ward and 378 private), the incidence was 1:57 in the ward cases as compared with 1:17 in the private cases. Thus we see that the old adage of safety in numbers still holds true.

The three main indications for cesarean were: contracted pelves, 240 cases (44.77 per cent); cephalopelvic disproportion, 82 cases (15.29 per cent); and placenta previa, 33 cases (6.15 per cent).

The type of operation preferred is the low segment transperitoneal which has the great advantage, among many others, of contributing markedly to the decrease in maternal deaths.

In the 536 cases of cesarean section, there were ten maternal deaths (1.86 per cent), constituting 22.72 per cent of the total obstetrical mortality. Deaths from hemorrhage, the chief cause of mortality, have been greatly lessened by means of an adequate preoperative replacement of the blood lost and the treatment of hemorrhagic shock.

From these findings, it is possible that our main faults in treatment have been the failure of securing early consultation, the finding of too many relative indications, the poor selection of the type of cesarean section, and the belated treatment of our hemorrhage cases. Nevertheless, with so many men operating, the final results are encouraging. Whenever there is only one man operating, he will get a low mortality for several hundred cases; whereas, in clinics in which there are many men operating, there is bound to be a higher mortality.

If we are to accomplish any improvement in the figures shown, a review of the errors in judgment, technique, and treatment must be undertaken from time to time and forcibly brought to the attention of the various operators. This is done at our hospital in the monthly conferences. The Maternal Mortality Committee of New York City, which at its monthly meetings carefully studies every maternal death, has also, through careful supervision and thorough analyses, been a great force in the improvement of our mortality rate.

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## Discussion

DR. PAUL TITUS, Pittsburgh, Pa.—Dr. Hennessy's series is from one hospital but from a group of 32 different operators, of whom 25 were members of the hospital staff, but perhaps not all in the Department of Obstetrics, while seven were courtesy staff members. How closely their indications and decisions could be supervised and controlled, and their varying operative ability supported by proper assistance is difficult to judge.

The general mortality rate following cesarean is still much higher than necessary throughout the country. It can and must be improved. While this risk continues, with some abatement but still with more hazard than there should be, the indications for cesarean have been greatly broadened and its incidence greatly increased.

Hennessy has some interesting figures bearing on this subject. In 1932, for example, their incidence was one cesarean in forty deliveries; by 1946 the rate had become one in twenty-four. He cites their total death rate for the fifteen years as 1.8 per cent. Seven of these deaths were in the first 5 years, 2 in the second, and only 1 in the third five-year period. He did not point out the creditable fact that 345, or more than half of their total cesarean sections were done in the third five years, so that their record for results has shown an even more striking improvement than appears at first glance.

In our smaller clinic but with a closely knit divisional staff group, we have shown the same tendency toward less rigid indications and more cesarean sections. Hennessy's paper induced me to study our own figures and I find that our incidence of operation has become definitely too high. Our maternal death rate during the same fifteen-year period as Hennessy's report was 0.84 per cent, but even that low figure shows that the conditions for which cesareans are done and the operation are still a dangerous combination.

To show the changing trend, I recall in a paper in 1939 being quite critical of cesarean section for delivery of twins, on the ground that they are smaller and always less likely to show disproportion even with small maternal pelves. I have now to admit, somewhat boastfully, to having done a cesarean section recently at Latrobe, Pa., for quadruplets. I hasten to add, however, that the patient had had a secondary trachelorraphy with scar tissue deposit, and was given a seven-hour trial labor before the operation.

We have a required consultation rule for all obstetric cases showing even minor complications. This is enforced and is definitely not "mere polite agreement." Operative privileges are restricted, and both consultations and operations are supplied without charge to these patients of our courtesy staff or restricted medical patrons of our Hospital.

These men have found this an agreeable "postgraduate course" in obstetric complications, applied to their own practices, and do not, nor could they, take exception to the regulations.

By long custom, it never even occurs to members of our general hospital staff, holding surgical privileges, to undertake a cesarean section. They do general surgery better than we do; do obstetric surgery better than they; we all agree and adhere to this and that is the end of the matter, by unwritten and friendly agreement and cooperation. Why this cannot be so in all hospitals I cannot understand, and I might add in passing that this same staff arangement holds with us for gynecology also. Nevertheless, with all these restrictions, our increasing incidence of sections has made it necessary for us to establish as a routine part of the weekly formal rounds a detailed review of every cesarean section case.

Several other outstanding points in Dr. Hennessy's paper should be referred to for special note because of their interest.

He emphasizes x-ray of the pelvis before or during labor, especially when disproportion is apparent. He appreciates that borderline pelves are one's greatest problem. His three main indications for cesarean section are contracted pelvis (44 per cent), cephalopelvic disproportion (15 per cent), and placenta prevìa (6+ per cent).

He cites an unusually good record of no newborn or maternal deaths in sixteen extraperitoneal cesarean sections, done for entirely valid reasons, including some instances of neglected or protracted labors.

He surprised me with a report from the literature of thirty-seven instances of uterine rupture following previous low flap cesareans (four of these before labor). He surprised me, also, with his own report of ten classic type cesareans in the eighty-one so recent as 1946.

The use of the Voorhees bag for any type of placenta previa is not even debatable, in my opinion.

Hennessy found the chief cause of cesarean deaths to be hemorrhage. In our clinic we have decreased the risk of this, as he has, by plasma and blood transfusions; also, by adopting Phaneuf's suggestion of the transverse incision in the lower uterine segment and by deliberate control of bleeding sinuses by a special clamp.

Hennessy's chief suggestions for lessening the death rate following cesarean sections are excellent. These are rigid though broadening indications and their control by competent consultation before any cesarean, assurance of competence in performance of the operation, and control of blood loss.

DR. ROLAND S. CRON, Milwaukee, Wis.—For many years we have been interested in the cesarean section problem, especially as it pertained to the County of Milwaukee as well as to the State of Wisconsin. At one time it appeared that the City of Milwaukee had one of the highest section rates of any large city in the nation. In one large private hospital the incidence ran as high as one in five deliveries.

A recent survey made of the performance at Milwaukee Hospital (private) and Milwaukee County Hospital (indigent and emergency) will be used as a comparison for the one presented by Dr. Hennessy. From the years 1933 through 1947, there were 19,883 deliveries at Milwaukee Hospital with 1,144 cesarean sections for an incidence of one in seventeen, or 5.7 per cent. Dividing this fifteen-year period into five-year intervals, the study shows that there was a 100 per cent increase in deliveries for each period but a very definite reduction in the incidence of sections from 7.4 per cent in the early period, to 5.5 per cent in the last one. Our most common indication for section has been a previous cesarean. We practice the dictum of once a cesarean always a cesarean. Our results prove the efficacy of that procedure. There have been no ruptured uteri and no deaths in the last 573 operations. Almost one-half, or 43.6 per cent, of this group were repeat sections. During the fifteen-year period there were ten deaths, giving a gross maternal mortality of 0.8 per cent.

We consider an incidence of 5 per cent to 5.5 per cent the irreducible minimum to which this operative treatment can be reduced. A rate lower than that we feel will produce a higher stillbirth and neonatal death rate, and there will result severe, and sometimes irreparable, damage to maternal soft parts.

The stillbirth rate was 2.1 per cent and neonatal deaths were 3.9 per cent.

The classical type of operation has been abandoned and the extraperitoneal found unnecessary.

Only certified obstetricians are now permitted to perform cesareans. There were twelve board members who did 560 of the last 573 sections performed.

The record at the Milwaukee County Hospital for 1943 to 1947 shows a much lower incidence of sections, namely, one in 48, or 2.5 per cent. Again, repeat sections were the most common indication. The low segment operation, with one exception, was the type of operation utilized. There was one death from bronchopneumonia. This series is a small one and is a good example of what happens in an industrial community where, during periods of high employment, medical and surgical care improves. During the previous five-year period there were 7,702 deliveries with 120, or 1.5 per cent, sections and eight deaths, or 6.6 per cent mortality.

In both institutions we have abandoned the use of caudal anesthesia because of two deaths and other complications attributed to that procedure. More and more we are relying upon Pentothal induction and gas for general anesthesia.

We concur with Dr. Hennessy's opinion that fewer sections are done on the indigent patients. On the other hand, we found both a higher maternal and fetal mortality in this group.

We found that the establishment of a city-wide ironclad rule that a free compulsory consultation by a certificated staff member would satisfactorily adjust our section problem.

Dr. Hennessy has intimated, and we have proved, that with the restriction of operators to only qualified obstetricians, and with the performance of the low segment operation, the maternal mortality can be reduced to a negligible factor.

Dr. Hennessy is to be congratulated on his excellent presentation of a very timely subject. I appreciate the amount of time and effort expended in preparing his paper.

DR. C. O. McCORMICK, Indianapolis, Ind.—The two entries of a cesarean section report that always attract our attention primarily, are the incidence of the operation and the maternal mortality. This is largely true because these two factors are the more or less generally accepted criteria used in judging the quality of obstetrics practiced in any given clinic.

Seeking a national mean of each of these two items, I have prepared a slide showing the respective figures, covering the five-year period 1941 to 1945, inclusive, gathered from twenty leading American clinics (Table I).

TABLE I. RECENT CESAREAN STATISTICS AS TO INCIDENCE AND MATERNAL MORTALITY (TAKEN FROM TWENTY OF THE LEADING AMERICAN CLINICS) 1941 TO 1945 INCLUSIVE

| CLINIC | TOTAL NUMBER OF DELIVERIES | CESAREAN SECTION | | | |
|---|---|---|---|---|---|
| | | NUMBER | INCIDENCE PER CENT | MATERNAL DEATHS | MORTALITY PER CENT |
| Boston Lying-in | 14,646 | 522 | 3.55 | 3 | 0.57 |
| Chicago Lying-in | 14,101 | 616 | 4.37 | 2 | 0.32 |
| Cincinnati University | 11,375 | 90 | 0.79 | 2 | 2.22 |
| Cleveland Maternity | 20,476 | 1,128 | 5.50 | 7 | 0.62 |
| Duke University | 5,648 | 105 | 1.85 | 1 | 0.95 |
| Emory University | 11,463 | 59 | 0.51 | 1 | 0.17 |
| Georgetown University | 8,408 | 192 | 2.28 | 0 | 0.00 |
| Illinois University | 3,275 | 118 | 3.60 | 3* | 2.54 |
| Iowa State University | 5,045 | 103 | 2.04 | 0 | 0.00 |
| Johns Hopkins | 9,350 | 455 | 4.86 | 1 | 0.21 |
| Los Angeles General | 15,289 | 559 | 3.65 | 11 | 1.96 |
| Margaret Hague | 33,981 | 902 | 2.65 | 6 | 0.66 |
| Mayo Clinic | 3,967 | 145 | 3.65 | 0 | 0.00 |
| New York Lying-In | 16,351 | 535 | 3.27 | 2 | 0.37 |
| Pennsylvania University | 11,893 | 840 | 7.06 | 3 | 0.35 |
| Providence Lying-in | 23,662 | 746 | 3.15 | 2 | 0.26 |
| Stanford University | 6,836 | 429 | 6.26 | 0 | 0.00 |
| Texas University | 4,556 | 123 | 2.69 | 1 | 0.81 |
| Tulane University | 10,460 | 224 | 2.14 | 5 | 2.23 |
| Washington Univ. (St. Louis) | 13,587 | 227 | 1.67 | 0 | 0.00 |
| Summary | 244,369 | 8,118 | 3.32 | 50 | 0.61 |

*Two of these deaths followed antemortem sections.

It is noted that the average rate of incidence of cesarean section of these twenty clinics, reporting a total of 8,118 sections in a total of 244,369 deliveries, is 3.32 per cent; and that of maternal mortality, .61 per cent. From this we may deduce that leading American clinics do have creditably low rates of incidence of cesarean section and associated maternal mortality.

The corresponding figures, 3.44 per cent (1:29) and 1.86 per cent, given in Dr. Hennessy's report are favorably comparable, particularly since they represent a much longer period of study during the major part of which certain techniques and many modern forms of therapy were unknown.

When we analyze his data of the same five-year period, 1941 to 1945, inclusive (Table II), we observe that while his incidence of the operation (4.22 per cent) is fully 25 per cent higher than that of the twenty clinics (3.32 per cent), his mortality rate (0.33 per cent) is approximately but half that of the clinics (0.61 per cent).

TABLE II. INCIDENCE AND MATERNAL MORTALITY OF CESAREAN SECTION
ST. VINCENT'S HOSPITAL, 1941 TO 1945, INCLUSIVE

| YEAR | DELIVERIES | SECTIONS | INCIDENCE | MATERNAL MORTALITY |
|---|---|---|---|---|
| 1941 | 1000 | 36 | - | 0 |
| 1942 | 1251 | 59 | - | 1 (Placenta previa—preventable) |
| 1943 | 1845 | 58 | - | 1 (Brain tumor—non-preventable) |
| 1944 | 1647 | 73 | - | 0 |
| 1945 | 1365 | 74 | - | 0 |
| | 7108 | 300 | 4.22% | 2—0.33% |
| Respective figures of 20 of the leading clinics 1941-1945 | | | 3.32% | 0.61% |

Many pertinent points arise in Dr. Hennessy's report. I will comment upon but a few of them.

1. Dr. Hennessy rightly stresses the growing importance of cesarean section in obstetric surgery. The incidence in his series doubled within fifteen years. While originally there was but one indication, fetopelvic disproportion, today that number has grown to approximately forty. Although the indications have greatly increased, the maternal mortality has decreased.

2. Relative incidence of cesarean section in private and ward patients. I am sure every staffman is aware that a definite disrelation on this basis exists in his clinic. Yet, I wonder if he knows just how great the discrepancy really is. Dr. Hennessy reports that in his clinic the incidence of the operation among private cases is more than three times that among ward cases—one in seventeen cases among the private, and one in fifty-seven cases among the ward patients—or 5.82 per cent against 1.75 per cent. In checking these two groups over the seven-year period, 1941 to 1947, inclusive, at our clinic at the Indiana University Medical Center, I was a little surprised to learn that we, too, had a ratio of over 3 to 1 (8.80 per cent : 2.80 per cent).

Personally, I question if such a discrepancy, and it no doubt exists more or less in all clinics, can be truly justified. Of course, there are bona fide factors that support to considerable extent this high disparity of over three to one. On the one hand, we have more elderly primiparas, more complicating disease because of greater age, a greater premium on fetal life, and so on; while, on the other hand, we are more often assisted by the ally youth, the importance of impressing upon students the value of conservative obstetrics, extending to students and the intern staff the privilege of observing protracted labor, et cetera.

Yet, the degree of discrepancy, which is sufficiently great to suggest discrimination, leaves much to explain away. The embarrassment, if any, is not lessened when we realize the greater frequency of repeat sections performed among private than among public or ward patients. Irving reports that at the Boston Lying-in, the ratio is more than two to one. During the past five years, the ratio at our clinic has been a little over one and one-half to one (0.71 per cent to 0.46 per cent).

Suffice it to say, "polite" consultations should be eliminated from the private group, and more "anxiety" applied to the ward group. In dealing with the ward patient, let us give her the advantage of early consultation, and in addition, foster the teaching that it is better to see what she can accomplish rather than what she can endure.

3. The essayist is correct in recommending in doubtful cases the aid of x-ray study. He is also correct in stating its limitations. No diagnostic aid erroneously interpreted causes

a more unnecessary rise in cesarean section incidence than the x-ray. The roentgenologist should be expected to give neither advice nor prognosis, but only his findings.

4. I find myself in agreement with the speaker in not being able wholly to endorse the dictum, "Once a cesarean, always a cesarean." However, this policy has been adopted by some of our larger clinics, and is finding favor with more and more operators.

Nevertheless, personal experience prompts me to be a little less radical. The late Dr. Stander of the New York Lying-In reported in 1944, 41 per cent of 360 previously sectioned cases in that institution as having been safely delivered from below.

In handling previously sectioned cases, two things should be kept ever in mind: (1) All such cases should be hospitalized. (2) Such a uterus should be allowed to withstand only the strain of pregnancy and the first stage of labor.

5. Dr. Hennessy's specified indications for the various types of section are for the most part well taken. While the classic operation may be the better choice in a few selected cardiac cases, it must be remembered that, as a group, cardiacs do not as a rule tolerate well section delivery, particularly the classic type. Also, in dealing with a placenta previa and an undilated cervix, I personally would not insist that the fetus be alive or at term. Better surgery dictates, "Molest a bleeding site the least possible."

6. It must be admitted that the usefulness of the extraperitoneal section even with its improved techniques is in general being much restricted by the success of the transperitoneal low segment operation, augmented by intravenous fluids, blood transfusion, antibiotics, sulfonamides, and abdominal decompression.

7. Dr. Hennessy's study brings forth the usual high gross fetal mortality of 10 per cent, which again reminds us that abdominal delivery cannot guarantee a living baby. Even normal-appearing babies breathing spontaneously not infrequently die a few hours after birth. Russ and Strong have demonstrated that direct tracheal aspiration of section-born babies produces 3 to 7 c.c. of mucoid material, and that of babies born per vaginam only 1 to 2 c.c. By adopting routine immediate intratracheal aspiration upon cesarean-born babies, they have reduced the death rate 80 per cent.

8. Two findings in Dr. Hennessy's study that run counter to general experience and customary teaching are the absence of maternal deaths in cases having more than twenty-four hours of labor and in cases having ruptured membranes.

DR. JOSEPH D. O'CONNOR, Worcester, Mass.—In regard to the incidence of section, Dr. Hennessy has stated that it is higher in private than in ward cases, a trend which is enhanced in no small measure by the anxiety hazard which confronts the obstetrician in cases where the element of friendship for the patient or her family inhibits the impersonal calm one may invoke with total strangers. It seems inevitable, therefore, that the incidence of section will be greater in hospitals where the census of private obstetrical admissions greatly exceeds that of the ward service. As a corollary to this thesis, the differences in the two types in physical and in nervous stamina undoubtedly play an important role in the incidence of the operation. The ability of the lethargic, rugged ward type of patient to endure the pain and effort of labor better than the educated, highly emotional, and frail private patient is well recognized.

Any attempt to elaborate on the excellent discussion by my predecessors on the indications for cesarean sections would be to "paint the lily." One finds it difficult, however, to refrain from observing that the number of indications for the operation is now legion, a condition probably begotten, in great measure, by an unwarranted fear of a stillbirth and the greater ease and safety of our present techniques of operation. Putting the brakes on this trend is no easy matter. Better teaching and training in the use of forceps at the higher pelvic levels are needed, and a better appreciation of the fact that cesarean section is not a panacea for all the problems of delivery.

The choice of operation still seems to be a moot question. While the classical operation has waned greatly in popularity, recent reported series of sections indicate that it is still too frequently invoked. It is much more deadly and a more frequent cause of morbidity than

the lower segment and extraperitoneal operations. The so-called low-flap transverse section is not only a relatively easy procedure but has, in addition to its safety and smoothness of convalescence, an amazingly low incidence of rupture of the uterine scar in subsequent pregnancies. An incidence of 0.26 per cent rupture of lower segment scars in a series of 3,600 sections of the low-flap type reported by Wetterwald, as against an incidence in this country variously reported as ranging from 4 per cent to 10 per cent of ruptures in classical scars is tragically significant. I am of the opinion that the extraperitoneal operation should be reserved generally, in the average clinic, for potentially infected cases.

A review of cesarean sections at the Memorial Hospital in Worcester during the fifteen-year period covered by Dr. Hennessy's paper shows that 821 sections were performed in 11,560 deliveries, an incidence of 7 per cent. There were three deaths in this series—one due to shock following abruptio placentae, one due to hemorrhage associated with placenta previa and the third, which occurred on the eighteenth postpartum day, due to pulmonary embolism. Two of these deaths followed low-flap operations. The mortality for the series was 0.036 per cent.

The sections were performed by six operators. More than 95 per cent were done by four obstetricians. In this series, there were three extraperitoneal sections, 59 classical sections and 762 low-flap sections.

The high incidence of cesarean sections in a hospital is probably due to: first, a top-heavy private service; second, the reference to the clinic as a consulting service of a number of potential cesarean cases; and finally, a clinic record of low maternal mortality.

DR. ALFRED L. POTTER, Providence, R. I.—Dr. Hennessy's results move me to ask that this Society help hold up the hands of others who are also trying to establish or maintain an "F.E.P.A.," a Fair Employment Practice Act for obstetrics—a reasonable and proper cesarean section incidence rate. With the authority of this organization behind us, those of us whose duty it is to direct them will better be able to control the *furor operandi* of more radical and inexperienced staff members of our hospitals.

By the same token I ask that, in the attempt to make Dr. Hennessy's results common elsewhere, this Society completely outlaw the use of the classical cesarean section. At the Providence (R. I.) Lying-in Hospital, in 47,885 confinements from 1938 to 1947, inclusive, there were 1,465 sections by 20 operators, an incidence of 3.1 per cent. Only thirteen classical sections were included, and even these were followed by the apologies required following the perpetration of any other equally grave social error. There was one death in the last 1,014 sections.

# THE ROLE OF PENICILLIN IN OBSTETRICS*

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PRIOR to the year 1935, sterilization of the blood by chemical means was looked upon as an unattainable ideal, and the occurrence of obstetric complications attended by infection constituted a major hazard reflected in high maternal and fetal morbidity and mortality rates. In 1935, the advent of the sulfonamides represented the first of the chemotherapeutic agents and probably the greatest therapeutic discovery in modern medicine. While the sulfonamides served as a powerful weapon for combating infections in general at a time when such a drug was so much in demand, there remained much to be desired to meet all the requirements, more especially those problems of infection in the field of obstetrics. It is believed, from experience gained thus far in its use, that penicillin will solve many of these problems.

## Relative Freedom From Undesirable Reactions

Experience with the sulfonamide preparations has demonstrated their limitations and contraindications in the presence of such conditions as severe anemia, nephritis, hepatitis, agranulocytosis and nausea, as well as their incompatibility with other drugs.

The purpose of this paper is to present some of the advantages offered by penicillin in the treatment of infections in pregnancy and its use in the management of obstetrical difficulties. From a review of the literature and from a study made during the past two years, it is desired to point out the wide therapeutic range of penicillin and its freedom from toxic and undesirable side reactions as well as its compatibility with other therapeutic agents.

Within the first year or two following discovery of the valuable antibacterial properties of penicillin and its use as a therapeutic agent, the question was raised by Stokes and others[1, 2, 3] as to its possible abortifacient action. It is significant that clinical observations made at that time of cases of threatened and actual abortion complicating the administration of penicillin in pregnancy were made in the early days of its usage and primarily on patients undergoing antisyphilitic treatment. It is now believed that those untoward reactions resulted not so much from the penicillin itself, but from the impurities contained in the commercial product prior to proper standardization.[4] It also seems significant that reports of the possible action of penicillin in stimulating uterine contractions to produce abnormal bleeding and premature labor were the result of observations made on patients under antisyphilitic treatment. Such reactions have since been interpreted as a "form of therapeutic shock or Herxheimer reaction."[5]

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In our experience there is nothing which suggests that penicillin has oxytocic or abortifacient properties. A summary of the fifty-eight patients who were treated with penicillin during their antenatal course is presented in Table I. The mode of administration in this series, as in nearly all of our patients, was the three-hourly intramuscular injection, and the penicillin used was crystalline penicillin G sodium in aqueous solution. As a result of reports in the literature by Hesseltine[6] and others, and from our own studies of blood concentrations and organism sensitivity, the administration of large doses, 50,000 to 100,000 units per injection, depending on the nature and severity of the infection, has been the established policy.

TABLE I. PATIENTS GIVEN PENICILLIN DURING PREGNANCY

| DIAGNOSIS | TRIMESTER IN WHICH PENICILLIN GIVEN | | | TOTAL PATIENTS |
|---|---|---|---|---|
| | 1 | 2 | 3 | |
| Syphilis | 2 | 4 | 0 | 6 |
| Cellulitis or furuncle | 2 | 2 | 1 | 5 |
| Otitis media | 2 | 0 | 0 | 2 |
| Pharyngitis | 2 | 3 | 0 | 5 |
| Upper respiratory infection | 1 | 2 | 1 | 4 |
| Acute appendicitis | 1 | 0 | 0 | 1 |
| Endocervicitis | 2 | 1 | 0 | 3 |
| Pelvic inflammatory disease | 7 | 1 | 1 | 9 |
| Vaginitis | 0 | 2 | 1 | 3 |
| Cystitis | 3 | 1 | 1 | 5 |
| Pyelonephritis | 0 | 3 | 6 | 9 |
| Miscellaneous | 0 | 1 | 5 | 6 |
| | 22 | 20 | 16 | 58 |

Of these fifty-eight patients, forty-two were in the first or second trimester of pregnancy at the time of treatment. None of these patients exhibited either vaginal bleeding or uterine contractions except three patients who were admitted with threatened abortion. Two of these patients were admitted with threatened abortion and received penicillin for concomitant pelvic inflammatory disease; neither patient aborted. The third patient, five and one-half months pregnant, was admitted with threatened abortion. She had had a polyp removed from the cervix at two and one-half months' gestation. She received penicillin treatment for an endocervicitis, and after three days of such treatment with continued bleeding she aborted a nonviable fetus. This is the only case in our series in which penicillin administration was followed by abortion, and it is at least questionable that penicillin could have been a significant factor in the termination of this pregnancy. We conclude, therefore, that penicillin, that is, the product available for use now, is not an abortifacient and does not have an oxytocic effect upon the uterus.

A review of the records of two hundred mature women patients with histories of normal menstrual cycles who were treated with penicillin revealed no incidence of abnormal uterine bleeding which could be attributed to penicillin therapy. Speiser and Thomas[7] made similar observations on thirteen hundred patients undergoing penicillin therapy.

### Bacterial Sensitivity and Mode of Administration

In cases of infection the importance of bacteriologic diagnosis of the invading organism cannot be overemphasized in view of the wide variations in penicillin sensitivity between various species or within the same group or strain. Clinical observations reveal that penicillin is more lethal for bacteria which stain gram positive than those which stain gram negative and more

effective against gram-positive and gram-negative cocci than against gram-negative bacilli. Table II lists some of the commonly encountered organisms with relative degree of susceptibility to penicillin.

TABLE II. SENSITIVITY OF COMMON ORGANISMS TO PENICILLIN

| VERY SENSITIVE (1) | SENSITIVE (2) | RESISTANT (3) | VERY RESISTANT (4) |
|---|---|---|---|
| *Corynebacterium diphtheriae* | *Streptococcus faecalis* | *Streptococcus pyogenes* | *Escherichia coli* |
| *Staphylococcus albus* | *Eberthella typhosa* | *Salmonella schott-mülleri* | *Pseudomonas fluorescens* |
| *Staphylococcus aureus* | *Salmonella parathyphi* | *Shigella dysentariae* | *Serratia marcescens* |
| *Neisseria gonorrheae* | *Brucella abortus* | *Neisseria catarrhalis* | *Aerobacter aerogenes* |
| | *Streptococcus hemolyticus* | | *Proteus vulgaris* |
| | | | *Klebsiella pneumoniae* |
| | | | *Haemophilus pertussis* |
| | | | *Monilia albicans* |

(1) Complete in vitro inhibition from 0.01 to 0.05 unit/ml.
(2) Complete in vitro inhibition from 0.1 to 2.5 units/ml.
(3) Complete in vitro inhibition from 5.0 to 20.0 units/ml.
(4) Complete in vitro inhibition requires 40 or more units/ml.

The degree of penicillin sensitivity is expressed in terms of the smallest number of units per c.c. of serum required to inhibit growth of the organism and may vary from 0.03 unit per c.c. to 20 or more units per c.c. Clinical observation and laboratory investigations indicate that penicillin resistance may rise with inadequate dosage. The objective in penicillin therapy, once procedures are started for bacteriologic diagnosis and sensitivity, is to establish and maintain a blood concentration above that considered clinically necessary to destroy the offending pathogen. In our experience maximal therapeutic efficiency has been obtained in the average infection by the three-hourly intramuscular injection of 50,000 to 100,000 units of penicillin in aqueous solution.

Blood level determinations have been considered of therapeutic significance in that they provide the following information: (1) when penicillin is present at maximally effective bacteriostatic concentrations; (2) when concentrations are lower, more slowly bacteriostatic concentrations are found; and (3) when concentrations are not sufficient to inhibit growth in vitro but great enough to act in vivo.[3] This explains the apparent discrepancy between reported in vitro sensitivities and the clinical response of the infectious process in many cases of infection with "resistant" organisms.

Penicillin differs in its action from that of the general protoplasmic poisons, such as certain halogens, heavy metals, and phenols, in that it interferes with a specific biologic mechanism in the growth process of a select group of organisms, causing ultimate destruction. The action of penicillin is exerted directly on the invading organism and is, therefore, not dependent upon interaction with the bodily defense mechanisms. Very high concentrations of penicillin may also be bacteriocidal to some organisms. Since penicillin has been found to be virtually nontoxic, it may be administered by any known avenue or route which will bring it in contact with the pathogen.

The intramuscular route is the method of choice in the average or more severe infections. On our service, all cases which require penicillin are admitted to the hospital in order that they may receive injections every three hours. The continuous intramuscular drip may be used in more severe infections where higher and more sustained levels are required.

Intravenous administration has been reserved for overwhelming infections where exceptionally rapid and high blood levels are desired. By the continuous intravenous drip penicillin enters the blood stream continuously and produces high levels despite its rapid excretion by the kidneys.

Subcutaneous administration of penicillin in aqueous solution is feasible with the highly purified crystalline preparations now available. The rate of absorption is slower than with the intramuscular and intravenous routes and blood levels are uncertain. There may also be pain at the site of injection.

Topical applications in the form of aqueous solutions or in ointment have a limited use, thus far, in obstetrics, due to local reactions, sensitization and uncertainty as to absorption and concentration. The study by Rock and associates[10] clarified the question and absorption per vagina. They have shown that except during the last two months of pregnancy therapeutic blood levels can be maintained by this mode of administration. A study of the use of vaginal suppositories for the prevention of postpartum morbidity has been recently reported by Pierce.[9]

## Results

In an effort to evaluate our results with penicillin treatment in infections complicating pregnancy, the records of one thousand consecutive admissions to the obstetrical service were reviewed. Cases not included here were admissions for observation of patients with such complications as toxemia, nervous disorders, and other conditions not on an infectious basis. These cases are presented in Table III. For purposes of comparison, all patients admitted with these diagnoses were included, whether or not infection was present.

TABLE III. 1,000 OBSTETRIC ADMISSIONS

| CASES ADMITTED ANTEPARTUM | PENICILLIN GIVEN | PENICILLIN NOT GIVEN | TOTAL |
|---|---|---|---|
| Abortion | 32 | 27 | 59 |
| Threatened abortion | 2 | 25 | 27 |
| Urinary tract infection | 16 | 4 | 20 |
| Genital tract infection | 9 | 0 | 9 |
| Syphilis | 6 | 0 | 6 |
| Incidental infections | 25 | 0 | 25 |
| Total this group | 90 | 56 | 146 |
| CASES ADMITTED INTRAPARTUM | | | |
| Normal | 0 | 736 | 736 |
| Mastitis | 24 | 0 | 24 |
| Genital tract infections | 20 | 3 | 23 |
| Urinary tract infections | 10 | 8 | 18 |
| Prophylactic penicillin | 27 | 0 | 27 |
| Incidental infections | 5 | 0 | 5 |
| Cesarean section | 14 | 7 | 21 |
| Total this group | 100 | 754 | 854 |
| Total both groups | 190 | 810 | 1000 |

Under "Abortion" are included all cases in which pregnancy was terminated before the age of viability and includes both complete and incomplete abortions. The classification, "Threatened Abortions," includes all cases within the first and second trimester admitted with vaginal bleeding, with or without abdominal cramps, and includes some cases in which infection was present. "Genital Tract Infection" includes all cases with infection

in the reproductive tract except those in which threatened abortion was the chief complaint. The group of "Incidental Infections" includes a variety of types of infection not related to the pregnancy except by coincidence. These are included in Table I.

The second category, "Cases Admitted Intrapartum," includes all patients who were delivered of a viable infant. Only those cases were considered to be "Normal" who exhibited no evidence of infection, did not receive penicillin or other specific chemotherapy, and who had no temperature elevation sufficient to be classed as "morbid." The group of genital tract infections includes pelvic cellulitis and perineal infections following episiotomy, as well as frank endometritis. Those patients listed under "Prophylactic Penicillin" received this drug for a variety of reasons; these indications are tabulated in Table IV. The classification, "Incidental Infections," again includes that group of patients who had infectious processes not related to the pregnancy, and all those in this category had upper respiratory infections.

"Cesarean Sections" are listed separately because it was felt that these constitute a special complication and that the results in these cases should be considered apart from the vaginally delivered patients.

TABLE IV. CASES RECEIVING PROPHYLACTIC PENICILLIN

| INDICATION | NUMBER CASES | AVERAGE DOSE | AVERAGE TOTAL | NUMBER MORBID | COMMENT |
|---|---|---|---|---|---|
| Antepartum gonorrhea | 1 | 30 | 1.5 | 1 | Temp. to 102° F. 3rd postpartum day, 101° F. 4th postpartum day, normal 4th postpartum day |
| Uterus packed | 9 | 60 | 1.4 | 0 | 6 patients temp. to 100° F. one day only |
| 3rd degree laceration | 4 | 80 | 2.5 | 0 | Afebrile, no signs of infection |
| Vaginal examinations before delivery | 6 | 40 | 0.6 | 0 | 2 patients, temp. to 100° F., one day only |
| Manual removal of placenta | 1 | 40 | 0.6 | 0 | Afebrile, gross contamination suspected |
| Premature rupture of membranes | 6 | 80 | 3.2 | 0 | 1 patient temp. rise to 100° F. one day only |
| Total cases | 27 | -- | -- | 1 | |

## Indications in Treatment and Prophylaxis

The various indications for the prophylactic use of penicillin in patients delivered vaginally are listed in Table IV. These twenty-seven patients constitute 3.2 per cent of the vaginally delivered cases. Only one patient had a morbid puerperium. She had acute gonorrhea during the eighth month of pregnancy, and received 30,000 units dosage of penicillin for a total of 3.2 million units during the acute phase of the infection with apparent recovery except for a moderately profuse nonspecific vaginitis. When this patient was admitted in labor, penicillin was again begun in 30,000 units dosage and was given for six days. In spite of this she had a morbid course with temperature to 102° F. on the third postpartum day and 101° F. on the fourth postpartum day with the usual signs and symptoms of acute endometritis. It is probable that the 30,000 unit dosage used at the time of delivery in this patient was inadequate, and suggests that some resistance to penicillin had been acquired by the organisms responsible for her vaginitis. This does not

reflect our current policy in this respect. During the past six months we have administered 100,000 units every three hours as the prophylactic dose whenever such prophylaxis was thought indicated. In general, the results as presented in Table IV were satisfactory since in all of these situations the likelihood of infection is, theoretically at least, much increased.

While it is true, as pointed out by Mengert,[11] that basic causes of intrauterine fetal death remain largely unknown, infection as a possible cause has received relatively brief mention in the literature. Again referring to Doctor Mengert's paper he listed infection as the cause of fetal and neonatal death in 8.1 per cent and 4.7 per cent in Sloane and Chicago Lying-in Hospitals, respectively.

In 1945, Douglas and Davis[12] pointed out the value of prophylaxis in puerperal infection over any known curative agent once the disease was established and stated at that time "that sulfadiazene or penicillin given early may be efficacious, while late in the course of the disease they may be relatively ineffective." Since then, some very interesting work has been done on the bacteriology of the uterus during labor and the puerperium. Guilbeau[13] and others on Doctor Eastman's service at Johns Hopkins Hospital have just completed a study of the effect of penicillin on the bacterial flora of the postpartum uterus. This investigation consisted of a study of the uterine cultures from eighty-six postpartum patients and indicates that relatively high doses of penicillin administered pre- and postpartum may eliminate penicillin-sensitive organisms from the postpartum uterus for seventy-two hours or longer. Even single doses, given early in labor, may be effective forty-eight hours after delivery. This very excellent work not only helps to confirm the opinion that penicillin therapy is more effective when instituted early, but will undoubtedly stimulate further interest in the study of the prophylactic use of penicillin in obstetrics.

TABLE V. CESAREAN SECTIONS

| | MORBID | | | | NOT MORBID | | | | TOTAL | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | | B | | A | | B | | TOTAL | MORBID | |
| | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT | NO. | NO. | PER CENT |
| Section during labor | 2 | 9.5 | 0 | 0 | 2 | 9.5 | 1 | 4.8 | 5 | 2 | 40.0 |
| Elective section | 3 | 14.3 | 1 | 4.8 | 7 | 33.3 | 5 | 23.8 | 16 | 4 | 25.0 |
| | 5 | 23.8 | 1 | 4.8 | 9 | 42.8 | 6 | 28.6 | 21 | 6 | 28.5 |

A, with penicillin.
B, without penicillin.

Table V lists the patients who were delivered by cesarean section. The section rate, 2.46 per cent, is comparable to the over-all section rate for this hospital, 2.66 per cent. It is interesting to note the increased morbidity among those patients who were sectioned after labor had started, namely, 40 per cent in that group, as compared to 25 per cent in the group sectioned electively before the onset of labor. This suggests that the onset of labor is a factor in the spread of infection as reported by Guilbeau. Most probably this related to the extension of pathogenic organisms from the lower reproductive tract to the interior of the uterus and probbaly also to the parametrial tissue. The incidence of morbid patients in this group who had received penicillin, as compared to those who had not, would seem to contradict our thesis that penicillin is efficacious in reducing the effects of an infectious

process. However, those patients who received penicillin were, for the most part, obviously infected before delivery was accomplished. Also, during the early part of the series relatively small dosages of penicillin were given, namely 30,000 or 40,000 units every three hours. Since we have begun to use large doses of penicillin, that is, 100,000 units every three hours, the results have been much more gratifying. This series of twenty-one sections is, of course, too small to permit any statistically sound comparison. It is, however, interesting to note that among the fourteen patients in whom there was an indication for penicillin treatment, only about one-third actually had a morbid postoperative course.

### Advantage of Adequate Dosage

Among the vaginally delivered patients, thirty-three, or 3.96 per cent, had puerperal morbidity (see Table VI). The largest group of morbidity was in a series of patients having mastitis. Two patients of this group were of special interest. These women had acute mastitis eight and eleven days, respectively, after delivery and were treated with 40,000 units of penicillin every three hours for a total of 800,000 units, and both had a fall of the temperature to normal within thirty-six hours. Both of these patients, however, had recurrences of the infection in the same breast within four days after the initial course of penicillin was discontinued. The second course of penicillin therapy consisted of 100,000 units every three hours for periods of four and five days, respectively. Both patients had a good clinical response and no further recurrences. We have noted that in cases of mastitis the most important factor as regards the duration of the febrile reaction and of course, concomitantly, the toxicity of the patient, is the time at which penicillin treatment was started, as was concluded by Douglas.[12] This factor seems to have been of more importance than the dosage. When penicillin was begun with the earliest signs of inflammation in the breast, the clinical course was much more benign than in those patients who had developed a marked febrile reaction before the onset of therapy. The infections cleared more rapidly, and there was less induration in the first group of patients. The dose of penicillin used seemed by and large to be related to the rapidity with which the inflammatory process resolved; that is, the period of convalescence was less and the duration of definite indurated areas was less in most patients receiving large doses. There was no case of recurrence in any patient who had received either 80,000 or 100,000 units of penicillin during the initial course of treatment.

TABLE VI. POSTPARTUM MORBIDITY

| DIAGNOSIS | NUMBER OF CASES | | | | TOTAL | |
|---|---|---|---|---|---|---|
| | MORBID | | NOT MORBID | | | |
| | A | B | A | B | NO. | PER CENT MORBID |
| Normal | – | – | – | 736 | 736 | 0 |
| Mastitis | 18 | 0 | 6 | 0 | 24 | 75 |
| Endometritis | 3 | 0 | 5 | 2 | 10 | 30 |
| Pelvic cellulitis | 2 | 3 | 3 | 0 | 8 | 63 |
| Perineal infection | 2 | 0 | 3 | 0 | 5 | 40 |
| Urinary tract infection | 2 | 2 | 8 | 6 | 18 | 22 |
| Prophylactic penicillin | 1 | 0 | 26 | – | 27 | 4 |
| Upper respiratory infection | 0 | 0 | 5 | – | 5 | 0 |
| Total | 28 | 5 | 56 | 744 | 833 | 3.96 |

A, with penicillin.
B, without penicillin.

We should like to note here that we are opposed to the practice of reducing the dose of penicillin when the acute phase of an infectious process has apparently been overcome. We believe that this will increase the incidence of recurrence since organisms beginning to develop a resistance to penicillin will not be affected when the smaller dose is used. It will be noted from Table VI that all patients with mastitis received penicillin treatment. In this small series of twenty-four cases there was no patient who developed abscess. It should be further noted that penicillin was the only specific treatment used in these cases; neither sulfonamides nor x-ray was employed as an adjuvant. We believe that the high incidence of morbidity in this group of infections in spite of penicillin treatment is only a reflection of the seriousness of the condition.

### Selective Action of Penicillin

The group of pelvic infections, i.e., endometritis, pelvic cellulitis, and perineal infection, is interesting in view of the response which these patients made to penicillin treatment. In endometritis the principal offending organism was *Staphylococcus aureus* in those cases which were not morbid and *E. coli* in all three cases which were morbid. It will be noted that these three patients all received penicillin. In perineal infections the organism was *E. coli* in both morbid cases and one of the cases which was not morbid, and a nonhemolytic streptococcus in the other two cases which were not morbid. Cases of pelvic cellulitis include those patients without definite signs of endometritis, but who did have lower abdominal tenderness and fever. In three cases large doses of penicillin were given with the onset of the earliest signs with a good response. In two patients penicillin was started only after two days of fever, and they also made a good clinical response. Three patients had relatively low grade fevers, 100.6° F. and 100.8° F. for two or three days with minimal signs, and were not treated with penicillin, but received sulfonamides.

Among the urinary tract infections, two out of the ten cases receiving penicillin were morbid. In these two cases sulfonamides were not given. In the eight cases which were not morbid, five had received sulfonamides and three had not. The two morbid patients with urinary infections who did not receive penicillin both received sulfonamide therapy.

The upper respiratory infections, five in number, all received penicillin treatment with the earliest signs of the disorder. All made excellent clinical response.

In reviewing these cases, several things seem to be suggested. First, in urinary infection, sulfonamides were apparently of more therapeutic value than was penicillin, even in large doses. Second, with a frank endometritis large doses given early were effective except in those cases in which *E. coli* was present, and in those penicillin seemed to be relatively ineffective. Third, in the group of perineal infections, the same situation obtains. This would seem to indicate that in postpartum infections the important factors are first, early treatment with adequate dosage of penicillin, and second, recognition of those cases in which a penicillin-resistant organism is present, and in such cases to use other drugs in addition to penicillin. We believe that penicillin is indicated in all cases of puerperal infection even when the principal pathogen present is known to be penicillin resistant. This means the effects of other organisms present will be kept at a minimum. Treatment should, of course, be instituted to combat the penicillin-resistant organisms.

## Pelvic Infection and Abortion

In our clinic we see a large number of patients who have pelvic inflammatory disease. Most of these patients have a relatively benign type of infection, chronic in nature, and these we classify as low grade types of infection. They rarely develop an acute exacerbation. It was our impression in the clinic and on the gynecological and obstetrical services, that many patients with this type of infection presented fertility problems and that abortions and threatened abortions were fairly frequent. It was thought, therefore, that perhaps the infectious process, per se, was a significant factor in these two conditions. If this were true, elimination of such an infectious process could probably be of benefit both as regards fertility and in the occurrence of abortion. We have no figures available on the effect, if any, of penicillin on patients with infertility problems, but it was possible to analyze our series of hospital cases of abortions, complete, incomplete, and threatened, with regard to the occurrence of concomitant pelvic inflammatory disease and in respect to the effect of penicillin treatment. These figures are presented in Table VII. It will be noted that eighty-six patients are included in this series. Of these, fifty, or 58 per cent, had clinically recognizable pelvic inflammatory disease, while thirty-six, or 42 per cent, did not. Among the first group of patients who aborted—including complete abortion or incomplete abortion necessitating dilatation and curettage—there were a total of fifty-nine cases. Of these fifty-nine, thirty-two patients had pelvic inflammatory disease and twenty-seven did not, or 54 per cent and 46 per cent, respectively. Among patients without pelvic inflammatory disease none received penicillin before abortion, and among the patients with pelvic inflammatory disease, only one patient had received penicillin before abortion (v.s.). In the group of patients with threatened abortions, nine were without pelvic inflammatory disease and eighteen patients had pelvic inflammatory disease. In the former group no patient received penicillin treatment. In the latter group two patients did receive penicillin.

TABLE VII. PELVIC INFECTION AS A FACTOR IN ABORTION

| | | A[1] | | | | | | | | B | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | TOTAL | | A | | B | | TOTAL | | A | | B | | A | |
| | | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT |
| Abortion | 59 | 1 | 1.2 | 1 | 1.2 | 0 | – | 58 | 67.5 | 31 | 36.1 | 27 | 31.4 | 32 | 37.3 |
| Threatened abortion | 27 | 2 | 2.3 | 2 | 2.3 | 0 | – | 25 | 29.0 | 16 | 18.6 | 9 | 10.5 | 18 | 20.9 |
| | 86 | 3 | 3.5 | 3 | 3.5 | 0 | – | 83 | 96.5 | 47 | 54.7 | 36 | 41.9 | 50 | 58.2 |

[1]Under "AB" only those patients are included who received penicillin before abortion occurred.

A, with penicillin.
B, without penicillin.
a, with pelvic inflammatory disease.
b, without pelvic inflammatory disease.

An analysis of these figures can only suggest a relationship since the series is very small but the suggestions are quite definite. The fact that there is a relatively small difference between the number of patients with and without pelvic infection who aborted would indicate that probably this infection was not the most important factor but that such abnormalities as defective ova and faulty implantation were more significant. However, among the patients with threatened abortion, the difference between these groups is considerable. Twice as many patients had pelvic infections as did not. This tends to sup-

port the hypothesis stated above. The study of this possible relationship is being continued on our service.

In view of the clinically proved value of penicillin when used alone or as combined therapy in not a few conditions which before its discovery were for the most part treated expectantly—and frequently unsuccessfully—a criticism that it is used promiscuously would seem unjustified. Until an antibiotic or chemotherapeutic agent with superior antibacterial activity and with equal freedom from toxicity is discovered, it is believed that penicillin administered for the proper indications, either prophylactically or early in the course of infectious disease, and in adequate dosage will continue to serve in revolutionizing the management of obstetrical problems attended by infection.

## Summary and Conclusions

1. The advantages in the use of penicillin in obstetrics over other chemotherapeutic agents are discussed, as well as its efficacy and compatibility with other agents in combined therapy.

2. The possibility of abortifacient or oxytocic properties of penicillin is discussed, and clinical evidence is presented which suggests that such reaction reported early in its use, for the most part in patients undergoing antisyphilitic treatment, was the result of impurities in the drug or of therapeutic shock.

3. The significance of bacteriologic diagnosis and sensitivity is discussed with their relation to dosage and therapeutic efficiency of penicillin. Penicillin resistance may rise in the presence of inadequate dosage.

4. The modes of administration and relative efficacy are discussed. The intramuscular route has been found to be the method of choice in all but the most severe infections.

5. An evaluation of the results of penicillin therapy in the various infections complicating pregnancy is presented in a statistical analysis. The value of the prophylactic and very early use of penicillin in sufficiently large doses when it is indicated has been fairly well established.

6. The possibility that pelvic inflammatory disease might be a factor in certain cases of infertility and in some cases of premature termination of pregnancy is suggested. While there are insufficient data from the study to prove such a thesis, further investigation may reveal that such infections are sufficient indications for active therapy. With our present armamentarium, this includes penicillin.

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## Discussion

Dr. R. T. LAVAKE, Minneapolis, Minn.—Drs. Harris and Shook have emphasized what our experience would corroborate: that pregnancy is not a contraindication to the use of penicillin, and that the earlier it is administered the more effective it tends to be, and that the dosage should be adequate from the beginning. The method of administration and dosage outlined has in our experience given excellent results.

Now in regards to when to stop the penicillin. We have found that it is well to continue the penicillin until all visual and palpatory signs of the inflammation have subsided and temperature and leucocyte count have been normal for forty-eight hours. It is hoped that there will be more discussion on this important point.

That the incidence of abortion is definitely increased by all types of infection is borne out by clinical experience; and serologic data has suggested the likely mechanism that brings about this increase. It seems, therefore, that the essayists are logical in their reasoning that by eliminating infection by penicillin the incidence of abortion should be reduced. The prevention and elimination of infection in pregnancy has been an essential part of prenatal care for many years, with the lessening of abortion incidence as one of its major aims.

It would seem from Dr. Harris's cesarean statistics that he wishes to make it clear that the idea of prophylactic penicillin should not lead one to change in any way one's rules governing the safest condition, method, and time for performing cesarean; and that the idea should not be interpreted as permitting any reduction in previously recognized standards favoring perfect asepsis or as permitting increased latitude in regard to the safety of operative interference. With these views we heartily concur.

It has been our experience also that urinary infections are most frequently of a type more amenable to the sulfonamides than to penicillin. Thus, the sulfonamides are tried first before results from cultures can be obtained and, if ineffective, penicillin is substituted.

DR. LOUIS DOUGLAS, Baltimore, Md.—Among the statements which Dr. Harris makes there are several which will bear repeating for the sake of emphasis: First, penicillin is not a panacea for all types of infection met with in obstetrics. There are organisms which are extremely resistant to the drug and little or no benefit would follow its use when dealing with infections from these. Therefore, cultures should be obtained at the onset of treatment and additiontal therapy added when indicated or, better still, since the colon bacillus is so frequently encountered, one of the sulfonamides might be included at the beginning of treatment. This is a point which has been and still is woefully neglected in many places. When the essayist speaks of the prophylactic use of penicillin, it would appear that he has learned well the inadequacy of small doses and at the present time is actually using it therapeutically; and this is as it should be. When a patient is potentially or actually infected, it means that her tissues are being invaded by pathogenic organisms of unknown virulence and susceptibility to penicillin. Since it is safe to use, in large dosage, it would seem better judgment to give enough to care for all contingencies. In this way there will also be much less danger of resistance to the drug occurring.

Captain Harris, when he speaks of cesarean section, does not state whether these were classical, low, or extraperitoneal, and in this he is probably wise since the relative safety of these various approaches is still being debated. Probably the simplest conclusion today is that, in the presence of infection, any type of section is hazardous, and that the sulfonamides and penicillin have materially reduced the risk but have not completely eliminated it.

The experiments in the use of penicillin in cases of relative sterility and repeated abortions are most interesting and it is to be hoped that the work will be continued. It might be extended with benefit to include the husbands as well as the wives.

DR. E. D. PLASS, Iowa City, Ia.—In an attempt to determine the effectiveness of penicillin given during labor in reducing the incidence of puerperal febrile reactions, my associate, Doctor W. C. Keettel, carried on a clinical experiment during the year ending in

February, 1948. Alternate patients were given 300,000 or 600,000 units of penicillin in oil and wax as soon as they were definitely in labor, and 300,000 units every twenty-four hours thereafter until delivery, with a single 300,000 unit dose post partum, twenty-four hours after the last antepartum injection. There were 465 patients in this series and 430 in the control group which received no antepartum antibiotics.

All temperatures were taken by mouth five times daily, every four hours except at 2:00 A.M. Any elevation to 100.4° F. or higher was considered febrile. "One-day fever" was diagnosed when the elevation persisted for less than twenty-four hours. The same criterion was employed in determining "intrapartum fever."

There was no significant difference in the incidence of "one-day fevers" and "intrapartum fevers" in the two groups, possibly indicating that they are not commonly due to infections, or that, if infectious in origin, the etiologic organisms are not penicillin sensitive.

Two-or-more-day fevers occurred in 10.2 per cent of the control series, as against 7.0 per cent in those receiving an initial penicillin dose of 300,000 units, and 3.0 per cent for the series given 600,000 units at the onset of labor. In the whole series there were twelve untreated patients who had fever for more than three days, as compared with only two in the treated series. This appears to indicate that the more persistent puerperal fevers are more likely to be due to aerobic gram-positive bacteria that are sensitive to penicillin. The evidence also appears to support the concept that a fair proportion of postpartum infections of the generative tract are the result of the invasion of anaerobic bacteria that genrally are resistant to penicillin.

This work is being continued in an effort to determine whether there is any value in prophylactic administration of this antibiotic to normal women with the prospect of normal parturition. At present, we are skeptical. On the other hand, we are already convinced that in prolonged labor, the exhibition of penicillin is reasonable and probably useful, particularly for the protection of the child from the dangers of amnionitis.

On the basis of our limited experience, we are also impressed by the value of antepartum penicillin injections as a means of eye prophylaxis in the newborn. Conjunctivitis neonatorum appears to be less common following this form of indirect prophylaxis than after local applications of either 1 per cent silver nitrate solution or of penicillin-containing ointment.

DR. NICHOLSON J. EASTMAN, Baltimore, Md.—On Jan. 1, 1947, we initiated a study on the efficacy of penicillin as a substitute for silver nitrate in the prophylaxis of gonorrheal ophthalmia. The object of that study, of course, had to do with ophthalmia and not with puerperal infection, but we were interested to know the results with regard to the latter. Each mother received 200,000 units of penicillin intramuscularly at the onset of labor. If her labor extended beyond eighteen hours, this was repeated. Our puerperal morbidity in 1947, judged by usual standards, was 3.8 per cent. In 1946 our puerperal morbidity had been 8.2 per cent, and in 1945, 9 per cent, and has never been below a figure of 8 or 9 per cent except for the year of 1947.

After trying to explore other explanations for this reduction of puerperal morbidity by one-half, we felt that the injection of penicillin was probably the factor. Some plausibility to this hypothesis was lent by the following circumstance. On Jan. 1, 1948, we gave up the maternal injection of penicillin in labor and, for the first six months of this year, our puerperal morbidity has returned to the previous figure of 8 or 9 per cent. This is in agreement with Dr. Plass's report, and it was this clinical study that led us to the laboratory and prompted the study that Dr. Guilbeau and his associates made and which Dr. Harris referred to this morning. They found that puerperal uterine cultures were sterile in 75 per cent of patients to whom penicillin had been administered routinely in labor, whereas in patients who had not received penicillin the great majority showed pathologic organisms. This leads us to believe that penicillin is lethal to most organisms that commonly cause puerperal infection. The clinical implications are plain enough; and it is our feeling that any woman who has been in labor for eighteen hours or more, or any woman who has ruptured membranes for

twelve hours or more, or who in any way seems to be headed for trouble, should have penicillin administered prophylactically. This is especially advisable if there is any likelihood of cesarean section being performed.

DR. OTTO H. SCHWARZ, St. Louis, Mo.—Bacteriologic studies done years ago, not only in our clinic but at New York Lying-In, Hopkins, and Chicago Lying-in, showed very conclusively that anaerobic streptococci are the chief offending organisms in such services. I have for some time made an effort to find out just what the penicillin would do to the anaerobic streptococci and found nothing definite. Sulfonamides are of no use against anaerobic streptococci. Dr. Plass stated that they are not sensitive to penicillin, and Dr. Eastman pointed out they were. This causes further confusion, but since Dr. Eastman's statement is based on actual bacteriological work, we must accept it.

DR. HARRIS (Closing).—Dr. LaVake has raised the question as to what constitutes adequate penicillin therapy. In our experience the indications for discontinuing the drug after the acute signs and symptoms of infection subside depend upon the condition. We believe the practice of reducing the dosage when the acute phase has apparently been overcome will increase the incidence of recurrence, since oganisms which develop a degree of resistance to penicillin will not be affected by the smaller dose.

In reply to Dr. Douglas: All our cesarean sections were of the low cervical type except one classical in a patient who had a history of a previous classical section.

From the interesting work they are doing with penicillin in obstetrics, the remarks by Dr. Eastman and Dr. Plass are a real contribution.

# CONTINUOUS SPINAL ANESTHESIA IN CESAREAN SECTION*

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DURING the past decade there has been a very marked improvement in the scientific management of women during pregnancy and parturition, which has resulted in a noticeable decrease in maternal mortality. A report of one thousand cesarean sections performed under one type of anesthesia presents only a part of this general picture and a few of the more pertinent factors which our study elicited are shown in Table I.

TABLE I.

| |
|---|
| *In the last ten years there has been:* |
| a 72 per cent decrease in over-all maternal mortality. |
| a 91 per cent decrease in maternal mortality from infection. |
| a 77 per cent decrease in maternal mortality from hemorrhage. |
| a 73 per cent decrease in maternal mortality from toxemia. |
| a 23 per cent decrease in maternal mortality from heart disease. |
| *Among cesarean sections in the last ten years there has been:* |
| an increase of 127 per cent in the use of low-type sections. |
| *From 1943 until the present there were:* |
| 0 maternal deaths from infection. |
| *In the last five years there were:* |
| 0 maternal deaths from hemorrhage. |
| *In the last 1,628 cesarean sections there have been:* |
| 0 deaths from anesthesia. |

It is noted that in the last 1,628 cesarean sections performed, there has been no death attributable to anesthesia. The last death from anesthesia occurred in 1938, when a very high-strung, nervous individual was given Avertin before being taken from her room to the operating theater. This patient died very suddenly while being transferred to the operating table. Following Lemmon's introduction of fractional spinal anesthesia into general surgery in 1939, we began to consider its use in cesarean section. Our experience with single-dose spinal had not been too satisfactory and we had discontinued its use about ten years prior to this date. During this interval we had performed most of our cesarean sections, when possible, under local or some form of general inhalation anesthesia, usually nitrous oxide and oxygen. It had been our experience that most of the babies born to mothers who had been deeply anesthetized, particularly with ether, at the time of cesarean section, had to be resuscitated immediately following birth, while those babies born to mothers who had local infiltration anesthesia for cesarean section, usually cried immediately. It was, therefore, more in the interest of the baby, than for the sake of the advantages to the mother, that we began in 1941 to use fractional spinal as the anesthesia of choice in our cesarean section patients. Up to June 1, 1948, we had performed 1,000 cesarean sections using this technique and it is our purpose

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in this communication to report our results. During this time we were also developing the use of continuous caudal analgesia in vaginal delivery and we extended its use to cesarean section in 162 patients, without a maternal death. We decided, however, that the continuous or fractional spinal was more applicable because of its simplicity of technique and the saving of time in waiting for the anesthetic level to be reached before operation could be performed. In using continuous caudal analgesia, an average of thirty-one minutes elapsed between the initial injection and the time the patient was ready to be moved to the operating room. In the use of spinal anesthesia there is usually only a waiting period of eight or ten minutes. Our results in continuous caudal, as previously reported, were satisfactory from the standpoint of both the mother and the child. During the period from January 1, 1941, to June 1, 1948, cesarean section was employed as the method of delivery in 1,378 patients. Because this communication is a report of our observations of continuous spinal anesthesia, we shall disregard an analysis of the 378 patients to whom other types of anesthesia were administered.

TABLE II

| | |
|---|---|
| Total number of deliveries | 18,980 |
| Total number of cesarean sections | 1,378 |
| Incidence of cesarean sections | 7.2% |
| Total incidence of cesarean sections from 1929 to 1948 | 6.3% |

Our incidence of cesarean section during this interval of seven and one-half years was 7.2 per cent, while the incidence for the nineteen years between 1929 and 1948 was 6.3 per cent. This incidence of cesarean section is high when compared with other statistics and there are several relevant factors which we believe should be pointed out. Our hospital admissions in this Division average about 65 per cent private patients and 35 per cent ward or service cases. Our staff is composed entirely of men who are recognized in our community as specialists and, therefore, a large number of patients are referred to them by outside physicians who have already recognized some abnormality necessitating abdominal delivery. Furthermore, during the last ten years we have increased our incidence of cesarean section in both abruptio and placenta previa and, contrary to opinions expressed recently by well-known authorities, our tabulated results showed an improvement over the results obtained by the more conservative treatment of these conditions. Again, we have increased our incidence of cesareans in pre-eclamptic toxemia where interruption of the pregnancy becomes a necessity and where the baby is almost always premature. We believe that cesarean section in these patients has been directly responsible for the salvaging of many more of these premature babies. We have also adopted the policy of doing a repeat cesarean in most cases, regardless of the indication for the first cesarean. For many years we did not adhere to the dictum, "once a cesarean, always a cesarean," and allowed many of our patients who had had a previous cesarean section for a temporary indication, such as placenta previa, to deliver vaginally. The stress and strain on the accoucheur during these labors and a few disastrous results from ruptured uteri caused us gradually to become believers in repeat cesarean sections. Occasionally, where the baby is small and the cervix is dilated or is easily dilatable, we do deliver the patient vaginally but the majority of subsequent deliveries are by the abdominal route.

In Table III we have shown the various types of anesthesia used but if we had included those patients operated upon under fractional spinal by members of our staff in other institutions, the series would total approximately 1,100 with no additional maternal deaths.

TABLE III. CESAREAN SECTIONS FROM JAN. 1, 1941, TO JUNE 1, 1948

| | |
|---|---|
| Performed under continuous spinal | 1000 |
| Performed under continuous caudal | 162 |
| Performed under general anesthesias | 174 |
| Performed under local infiltration | 5 |
| Performed under single injection spinal | 37 |

When we first instituted the use of fractional spinal we decided to confine ourselves to the use of only three drugs; not because we thought these three were more satisfactory than others on the market but rather in order to simplify and better control our study of this series. In some of our experimental work with caudal we found that procaine in Ringer's solution seemed to have a more lasting effect than either Metycaine or procaine hydrochloride.* Table IV shows the number of patients to whom these drugs were administered for spinal anesthesia.

TABLE IV. DRUGS USED IN CONTINUOUS SPINAL ANESTHESIA CESAREAN SECTIONS

| | |
|---|---|
| Metycaine, 1.5% | 692 |
| Procaine in Ringer's Solution | 194 |
| Procaine hydrochloride | 114 |

TABLE V. AVERAGE DROP OF SYSTOLIC BLOOD PRESSURE IN 1,000 CASES OF CESAREAN SECTION UNDER CONTINUAL SPINAL ANESTHESIA

| | |
|---|---|
| Metycaine (692 cases) | 13.0 mm. of mercury |
| Procaine in Ringer's Sol. (194 cases) | 1.5 mm. of mercury |
| Procaine hydrochloride (114 cases) | 11.5 mm. of mercury |

One of the most frequent complications that occurred when we were using single-dose spinal years ago was the development of marked hypotension. During our early use of continuous caudal and before we knew how to combat this condition, we noticed that the unborn child was definitely affected, as evidenced by the tumultuous movements which occurred in the uterus during the period of hypotension. We are not condemning single shot spinal because if it is given properly this complication can be avoided. Since the technique of administration has been refined and the drugs used today are less toxic, most anesthetists do not fear hypotension. It was our belief that if the patient were given small doses to begin with and then they were gradually increased until a satisfactory level of anesthesia had been obtained, there would be less opportunity for complications to develop. In most patients, any serious complication will usually develop within a period of five or ten minutes after the initial injection. Although it is contended that neurogenic fixation of these drugs occurs within from six to twenty minutes after they are administered, Hingson *et al.*,[1] in studying 100 patients who had fractional spinal anesthesia, removed several

TABLE VI. AVERAGE DOSAGE OF DRUGS USED

| | |
|---|---|
| All drugs | 65.9 mg. |
| Metycaine | 58.01 mg. |
| Procaine in Ringer's solution | 71.4 mg. |
| Procaine hydrochloride | 108.9 mg. |
| Number of cesarean sections done with 15 to 30 mg. of anesthetic drug | 71 |

*At our request, the Abbott Laboratory very kindly made up for us some procaine in Ringer's solution to be used in our study.

c.c. of spinal fluid at the end of the operation which were found to contain anywhere from 7 to 20 per cent of the drug used. Therefore, if a circulatory collapse should occur, the withdrawal of the spinal fluid would also remove part of the anesthetic agent. Table V shows the average drop in systolic pressure in this series.

Table VI shows the average dosage of the drug used. In this series there were 71 cesareans in which only 15 to 30 mg. of the drug were required for the entire operation. We gradually decreased our dosage with the idea that complication would be less likely to develop if less of the drug were used. This we believe is one of the advantages associated with the fractional method. It might be of interest to know that in this group of 1,000 patients, the anesthetic was administered by 38 different individuals, all of whom adhered rigidly to the technique as outlined. The technique of administering continuous spinal anesthesia is as follows:

One hour prior to operation, the patient is given 1.5 grains of the same barbiturate which was given as sedation the previous evening.

One-half hour before operation, the blood pressure is rechecked. If the systolic pressure is below 130 mm. of mercury, a vasopressor drug is given; usually three-fourths of a grain of ephedrine hydrochloride. We believe it is important to give the drug one-half hour before operation for the best results. Should the pressure be above 130 mm., no drug is given at this time.

When the patient is brought to the operating theater she is placed on her side, on a table upon which there is a special mattress designed by Dr. Lemmon.

Under aseptic precautions, the initial skin wheal is made with procaine, between the first and second, or second and third lumbar interspaces. A stainless steel safety needle is inserted into the subarachnoid space. With the needle in one of these interspaces, the drug will reach above the umbilicus and will produce the desired level of anesthesia with the minimum amount of dosage.

A 10 c.c. ampule of procaine in Ringer's solution is then opened and placed in the syringe. This is a 1.5 per cent solution of procaine containing 15 mg. per c.c. The syringe is then connected to the tube, which is filled with the solution to expel the air. The tube is then connected to the needle and the initial dose is given. The average initial dose is 15 mg.

The patient is then turned on her back and placed in a five-degree Trendelenburg position. The needle is then checked to determine whether it is still in the subarachnoid space. This is done by aspiration with the syringe. If no fluid is aspirated, the needle must be adjusted until there is a free return flow.

The length of time for the establishment of anesthesia is usually five to ten minutes, during which time the abdominal field is prepared and draped. If the level of anesthesia is not satisfactory, an additional 1 c.c. of procaine is given.

The blood pressure, pulse, and respirations are taken every five minutes during the operation.

The systolic pressure seldom drops more than 10 to 12 mm. and in many patients there is a drop of less than 10 mm. of mercury. If the systolic level reaches 90 mm. or less, three-fourths grain of ephedrine hydrochloride is given hypodermically and glucose in saline solution is given intravenously. Plasma should be available. If there is a persistent fall in blood pressure, the vasopressor drug is given intravenously

If the anesthesia begins to wear off or the patient complains of discomfort at any time during the operation, additional doses of procaine can be given, usually in 0.5 to 1 c.c. dosage, which represents 7.5 to 15 mg. of the drug.

During the past year and a half we have been starting a continuous drip solution of Pentothal sodium, 0.5 per cent, at the rate of 45 drops per minute when the operation begins. This quiets the patient but does not put her to sleep. Following the extraction of the child it is increased to about 90 drops a minute. This allows the patient to hear her baby cry and to know that he is all right. On increasing the dose of Pentothal she then sleeps through the

remainder of the operation but is usually awake when she leaves the operating table. An oxytocic drug, usuually a preparation of Ergotrate, is given as a routine procedure and the patient, while still on the table, is also given one-fourth grain of morphine. Upon her return to her room, the patient is placed flat in bed and allowed to have fluids and soft food on the day of operation.

TABLE VII. TYPE CESAREAN SECTION

| | |
|---|---|
| Low classical | 479 |
| Low flap | 452 |
| Extraperitoneal | 53 |
| Cesarean hysterectomy | 16 |

Table VII shows the various types of cesarean performed upon these 1,000 patients. The incidence of low section has increased 127 per cent in the last ten years. We do not do the low section as a routine procedure, particularly when the operation is elective and when a previous cesarean section has been performed, or when sterilization is to be carried out. Our results with the extraperitoneal type of operation have been extremely satisfactory and we believe this is the procedure of choice in potentially infected cases. We do not believe that cesarean hysterectomy is preferable to the extraperitoneal operation in these infected cases. Neither do we feel that hysterectomy is necessary in order to produce an effective sterilization. The cesarean hysterectomies performed in this series were upon patients who had complicating myomatous tumors.

TABLE VIII. INDICATIONS FOR CESAREAN SECTION

| | | |
|---|---|---|
| 1. Cephalopelvic disproportion | | 382 |
| 2. Pelvic tumors | | 30 |
| 3. Abruptio placentae | | 32 |
| 4. Placenta previa | | 62 |
| 5. Toxemia of pregnancy | | 42 |
| 6. Cardiac disease | | 18 |
| 7. Pulmonary disease | | 5 |
| 8. Kidney disease | | 4 |
| 9. Elderly nullipara | | 25 |
| 10. Recent or extensive vaginal plastic | | 40 |
| 11. Elective cesarean sections | a. Previous section | 268 |
| | b. Overvaluable baby | 14 |
| | c. Difficult previous delivery | 9 |
| | d. Uterine anomalies | 5 |
| | e. Prolapse of cord | 6 |
| | f. Diabetes mellitus | 2 |
| | g. Malpresentation | 40 |
| | h. Rh syndrome | 9 |
| 12. Dystocia syndrome | | 40 |
| 13. Prolapsed colostomy with obstruction | | 1 |
| 14. Uterine inertia | | 5 |
| 15. Leucemia | | 1 |

Table VIII shows the indications for cesarean section in this series. This classification of indications was adopted by our staff several years ago. All of our cases of cephalopelvic disproportion are x-rayed and the films are discussed by some member of both departments. Although we have increased the number of cesareans performed in abruptio and placenta previa, we do not believe that all of these patients should be delivered by this method. However, where there is any doubt, we perform a cesarean section rather than employ conservative treatment. Our incidence of cesarean section in cardiac disease has decreased considerably since the advent of the various forms of conduction anesthesia for vaginal delivery. In this group, 268 patients had had previous cesarean section. There were fourteen elective operations performed because of disastrous ex-

periences in previous vaginal deliveries or because the patient was in the late third or early fourth decade of life, and particularly where the fulfillment of the desire for offspring was of paramount importance. We performed nine cesareans because the mothers were Rh-negative and the fathers were Rh-positive, with change in the titers. At the present time we are of the opinion that if these patients had been allowed to go to full term and had been delivered vaginally, these babies would have been normal children and we would not have had to deal with the problem of prematurity. There were two patients with leucemia; one who comes under the classification of previous section, having had one section performed in another institution because of cephalopelvic disproportion, and one who had made several ineffectual attempts at going into labor and because of her rapid downhill progress it was thought best to terminate the pregnancy in this manner. As will be seen by this table, there were more than 1,000 indications for cesarean section. This is explained by the fact that in several instances there was more than one indication for the operation.

TABLE IX. NUMBER OF FAILURES UNDER CONTINUOUS SPINAL ANESTHESIA: 27

| | |
|---|---|
| Technical failures | 10 |
| Level not sufficiently high to proceed with operation, supplemental anesthetic necessary | 17 |

Among the patients who were scheduled for operation under this technique, there were 27 failures; ten were technical failures as the anesthetist was unable to insert the needle properly, and in seventeen a satisfactory level could not be obtained in spite of increased dosage of the anesthetic drug. In five of these seventeen patients, the needle had been dislodged in moving the patient and this was not recognized until after the abdominal incision had been made. Further instillation of the drug was not possible and a supplemental inhalation anesthetic became necessary.

The maternal mortality in this series included one case of leucemia, with the death occurring 12 days after operation. This patient had a rapidly progressing acute leucemia and death was due to this disease. Autopsy showed a perfectly healed uterine scar. Refinement of technique and emphasis on the choice of anesthetic, and the choice of the type of operation performed in these patients, will unquestionably give rise to the reporting of other large series with no maternal mortality. Waters[2] reports no deaths in the last 650 cases at the Margaret Hague Maternity. He ascribes the low cesarean mortality largely to the selection of the operation. In this we concur. The decrease also may be attributed to the development and use of the various antibiotic drugs but we are strongly of the opinion that it is a combination of choice of anesthesia and type of operation which is most important.

TABLE X. FETAL MORTALITY

| | | |
|---|---|---|
| 1. Stillborn | | 14 |
| a. Abruptio placentae | 9 | |
| b. Malpresentation | 4 | |
| c. Premature (7 months) death<br>Operation, twisted ovarian cyst | 1 | |
| 2. Neonatal | | 33 |
| a. Prematurity | 23 | |
| b. Cerebral hemorrhage | 1 | |
| c. Congenital heart disease | 4 | |
| d. Rh, erythroblastosis | 3 | |
| e. Hydrocephalus and spina bifida | 1 | |
| f. Congenital atresia of esophagus | 1 | |
| Total fetal deaths | | 47 |
| Uncorrected fetal mortality | | 4.7% |

Table X shows the fetal mortality. This was uncorrected and several of these babies were quite premature. In 986 babies born alive in this series, only one required actual resuscitation other than clearing out the upper respiratory passages. This occurred in a 6½ months' premature infant born to a patient who had a premature separation of the placenta. This baby died five hours after delivery but weighed only one pound, twelve ounces.

TABLE XI. MORBIDITY

| | |
|---|---|
| Endometritis | 77 |
| Pyelocystitis | 34 |
| Mastitis | 13 |
| Thrombophlebitis | 10 |
| Intercurrent infection | 13 |
| Dehydration | 2 |
| Morbidity—cause unknown | 12 |
| Wound infection | 21 |
| Atelectasis | 1 |
| Postoperative reaction | 26 |
| Transfusion reaction | 4 |
| Drug sensitivity | 1 |
| Total | 214 — 21.4% |

Table XI shows a 21.4 per cent morbidity, based on the standard of an elevation of temperature of 100.4° F. on any two days during the first ten days but excluding the first 24 hours after delivery or operation.

TABLE XII

| | |
|---|---|
| *Number of Patients Requiring:* | |
| 1. Intravenous glucose | 31 |
| 2. Supplemental vasopressor drugs | 238 |
| 3. Blood transfusion | 9 |
| *Distention:* | |
| Mild-moderate | 32 |
| Wangensteen drainage | 4 |
| *Headache:* Postspinal headache | 16 |
| *Neurologic Complications* | 0 |

Table XII is interesting from several standpoints. In this series we did not routinely give intravenous fluids except for a definite indication. Two hundred thirty-eight of these patients had developed sufficient hypotension to warrant the giving of supplemental vasopressor drugs. Nine required blood transfusions and were all patients with serious hemorrhage from abruptio or placenta previa. We have been particularly impressed by the small number of patients who suffered from distention following cesarean section. It was necessary to institute Wangensteen drainage in only four patients in this series of 1,000. Although the resident staff had been instructed to write on the record any incident of headache, there were only 16 postspinal headaches recorded. This figure we believe to be incorrect. We are sure that there were several more but the headaches were not of sufficient severity to be brought to the attention of the visiting staff. In reviewing our impressions concerning spinal headache occurring in conjunction with the single-dose spinal and with the fractional method, we feel that there has been a comparatively small number in this series. We hesitate to consider the possibility that the fractional method is responsible for this decrease in incidence of postspinal headache since we do not have accurate statistical data to substantiate our belief. We did not become spinal headache conscious until after we had used this method for two or three years. This postoperative complication, as we have seen it, is a troublesome one but as a rule is relieved almost immediately by the application of a wasp girdle or in-

sertion of an inflated rubber bladder under a tight binder. We have seen one or two instances in our gynecological service where the headache has been persistent over a period of several days and nothing seemed to relieve the patient except keeping her perfectly flat. At the present time we are delivering a large number of our obstetrical patients by the use of saddle block or terminal one-dose spinal and are attempting in this series to obtain much more accurate data concerning the incidence of headaches in these patients. In this series there were no neurological complications although there have been reports of serious complications in the nervous system following use of spinal. We believe that if the technique is meticulously carried out these complications will be reduced to a minimum and we feel very strongly that the use of either fractional or single-dose spinal anesthesia should not be condemned because these complications occasionally occur.

## Summary

We believe that our experience in studying this rather large series of patients, using the above outlined technique, has shown us many advantages of this method. The safety of continuous spinal anesthesia lies mainly in adhering to a rigid technique and we believe that the use of a smaller dose of the drug is an additional safeguard to the patient. This method also permits more controllability. The ease of administration allows it to be given by many different individuals, although we do not feel that a patient who has a spinal anesthetic of any sort should be supervised by anyone other than a trained anesthetist who has had experience in the use of all forms of conduction anesthesia. The excellent contraction of the uterine musculature with a minimal amount of blood loss is outstanding. The absence of narcosis in the baby offers one of the greatest advantages. This is particularly true where the baby is premature, as most of these will establish respiratory efforts almost before they are extracted from the uterus. Because of this fact, care should be taken to aspirate as quickly as possible the amniotic fluid which might be in the infant's mouth. Relaxation of the abdominal wall enables the operator to perform the operation with facility and dispatch. This type of anesthesia causes no disturbance of previously existing pathology in the respiratory, circulatory, or genitourinary system of the mother as the drugs used are low in toxicity and a minimal dosage is employed. The postoperative convalescence of these patients is marked by extreme comfort as compared with those given a general anesthetic and the postoperative complications such as distention and vomiting are kept at a minimum. We do not feel that the postoperative complication of spinal headache in this series occurred frequently enough to warrant criticism of the method used.

## Conclusions

Our analysis of 1,000 women delivered by cesarean section under fractional spinal anesthesia has demonstrated to us the following facts:

That, in addition to many other improvements in operative technique of which we are cognizant, fractional spinal anesthesia is definitely a safeguard to the operation of cesarean section.

That we should not condemn single-dose spinal anesthesia, as we know that, in proper hands, complications which may result from the large single-dose injection can be avoided. However, we do feel that a word of caution should be added when spinal is given by that method.

That we prefer the fractional spinal to the single-dose method because of its safety and the many advantages of administration which it affords.

That in order to bring our maternal mortality to an irreducible minimum we must surround all of our patients with every safeguard available. In cesarean section we believe that fractional spinal anesthesia is another safeguard.

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## References

1. Hingson et al.: Ann. Surg. **118**: 971, 1943.
2. Waters, Edw.: Pennsylvania M. J. **51**: 1093, 1948.

## Discussion

DR. S. A. COSGROVE, Jersey City, N. J.—This presentation is of special interest because it exhibits the qualities which make for a great clinic, that is to say, the restless search for constant betterment in method and in concept. There is perhaps no one who can better appreciate the extent of this shift of base over the years in relation to anesthesia, and I very sincerely rejoice with the authors of the paper on the extensive and discriminating work which they have done with a variety of forms of lower-neuron anesthesia and analgesia, and their ready acceptance of those techniques which from time to time appear to merit their confidence most. The decrease in general maternal mortality at the Philadelphia Lying-In is outstanding, and the very low postcesarean death rate is remarkable and commendable. The authors report an incidence of cesarean section of 7.2 per cent in a service which represents 65 per cent of private cases. It is hardly necessary for them to defend this incidence so extensively, because it is the same excuse we all use to justify a higher incidence of section in our private work than we permit our Residents to use in the Ward Service cases. The very decided shift toward the lower segment type of operation, the moderately extensive use of extraperitoneal section, and the practice of reserving cesarean hysterectomy for other indications than uterine infection are all salutary trends. About the only detail in the whole paper with which I do not concur is the plan always to do repeat sections on women who have had any kind of section, for any kind of an indication previously, in order to eliminate the "stress and strain on the accoucheur during these labors." I am interested that the Philadelphia experience has shown that for this work procaine is the most acceptable drug. I am also interested in the suggestion that this is best administered in Ringer's solution, although we have not personally had experience with this detail of technique.

For a considerable time we have been starting a continuous drip of glucose-sodium chloride solution before any spinal anesthesia is started. Not only does this appear to have the advantage of stabilizing the circulatory status, but it pre-establishes a channel through which vasopressor drugs, oxytocics, supplemental anesthetics such as Pentothal, plasma, and blood, may all be readily used as they may be indicated.

Finally, I want to stand shoulder to shoulder with Drs. Lull and Ullery in their advocacy of lower-neuron anesthesia for all the operations of obstetrics, in the interest of both the mother and the fetus. Neither I nor they care to dictate to anyone else the precise form of such anesthesia employed. Nor do we have the slightest interest whatever in forcing our own opinions and practices on others. I do hope, however, that the significance of this splendid presentation, with every essential of which I thoroughly agree, will not be lost on those who have so far failed to appreciate the advantages of these forms of anesthesia over those which so needlessly, and frequently so harmfully, obtund the higher cerebral centers.

DR. M. PIERCE RUCKER, Richmond, Va.—It has not been so very long when to have delivered 1,000 cases per vaginam with but a single death would have been considered a noteworthy feat. Drs. Lull and Ullery report a thousand cesarean sections with one maternal death and that from leucemia 12 days after delivery. Their fetal mortality, 4.7 per cent, also deserves comment. Furthermore, their series is unique in that the thousand sections were done under a single type of anesthesia.

There is one disturbing aspect of this report. It is so good that it will certainly stimulate others on the same scale. This will mean in many instances widening the indications for cesarean section in order to get numbers. For instance, our incidence of sections is less than 0.7 per cent. In order to get a thousand cases we will have to deliver 142,857 women or else widen our present indications. I wish to add one more indication to Dr. Lull's list and that is inadequate abdominal wall. In June of this year a multipara was admitted to the Sheltering Arms Hospital with a tremendous postoperative abdominal hernia and cellulitis of the abdominal wall. Her story was that 15 months previously an appendectomy had been done through a midline incision. When she began to get big with the present pregnancy the scar became black and soon the adjacent abdominal wall became inflamed. She was treated with compresses of normal salt solution and with penicillin and the cellulitis disappeared. She returned to the hospital in August. The whole uterus was in the hernial sac, and the overlying abdominal wall was very thin. The scar was still black and had begun to widen. Her temperature and pulse were normal. She was again treated with penicillin and compresses and on August 26 Dr. Edwin Rucker did a section under continuous spinal anesthesia, using procaine dissolved in spinal fluid. He made a lateral incision and after doing a low flap operation removed the redundant abdominal wall and repaired the hernia. The patient was out of bed the next day. She had an afebrile postoperative course and she and her baby were discharged in good condition.

There is another aspect of Dr. Lull's paper that fills me with envy and that is his ability to predict a prolapsed cord so as to plan an elective cesarean section. He had six such cases. If he will teach me how to do that, I will add that to my indications. Otherwise his indications for section are in the main the ones we have followed. We have not performed a section for heart disease nor have we done one because the patient had had a vaginal plastic operation. I believe we do fewer proportionately for placenta previa and the toxemias of pregnancy. On the other hand, we did in our small series actually more for diabetes mellitus than did Drs. Lull and Ullery. Most of our cases of diabetes are referred to us and are treated by a specialist in that disease. In some of them the gonadotropic hormones get out of control at about the 36th week, and in such cases we usually do a section.

In regard to the type of operation, our series since 1941, includes fourteen classical cesarean sections, thirty-one low-flap operations, and five extraperitoneal sections. One was done under nitrous oxide-ether, six under ether, eight under ethelene, three under intravenous Pentothal, two under local, ten under local with Pentothal for the uterine incision, and nineteen under continuous spinal anesthesia. One of our patients was operated upon in a neighboring city for premature separation of the placenta, and my notes in her case do not show what anesthesia was used. There were no naternal deaths. We had eight fetal deaths, including a nonviable 6 months' baby whose mother had advancing tuberculosis and another about the same age whose mother was pre-eclamptic.

I was interested to note that the authors noted no neurologic complications. None of our cases in which a section was done had such complications, but two patients who had been given continuous spinal anesthesia for vaginal delivery, developed spinal meningitis afterwards. Both developed the meningitis after their postpartum examination at the fourth week. Both were extremely sick, but fortunately recovered. In neither case could bacteria be demonstrated by smear or culture, and in neither case could the internist ascribe a cause for the disease. This occurred during the war when discussion of infectious hepatitis had made us virus-minded. If we assume that the spinal injection were the cause, the prolonged incubation period and the sterile cultures would suggest a virus infection. A 1 per cent procaine solution in normal saline was used in each case. The solution was sterilized in the

hospital by boiling and the tubing, needles, syringes, etc., were autoclaved. The skin was prepared with tincture of iodine and alcohol and the anesthetist used sterile rubber gloves. Since this occurrence, we have not used continuous spinal anesthesia for vaginal delivery, but I still think it the most satisfactory anesthetic for a cesarean section.

DR. LULL (Closing).—May I thank both Dr. Cosgrove and Dr. Rucker for their very kind discussion of this presentation. I was particularly anxious to have both of them discuss this paper because of their wide experience in the use of spinal anesthesia. We all look to Dr. Cosgrove as being one of the outstanding pioneers in this work. For many years I disagreed with Dr. Cosgrove concerning the use of spinal anesthesia, particularly in cesarean section cases. I now have reversed my opinion and agree most heartily with him and I believe the statistics as borne out in this presentation will show that it is probably the safest anesthetic both for the mother and for the child. Both Dr. Ullery, my associate, and I feel that the use of fractional spinal is another safeguard to the woman undergoing an operation for abdominal delivery. When we started this work in 1941 we felt that we did not want to make any definite report on our findings until we had had a sufficiently large group of patients and we therefore set arbitrarily on the number as being one thousand. As our series progressed we found that the many factors which were so satisfactory, such as small amount of blood loss, the baby being in such good condition, and the quick recovery of the mother, were so pronounced that it is only occasionally that we resort to any other type of anesthesia.

# ELDERLY PRIMIGRAVID WOMEN*

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AMONG primigravid women the problem of age and aging in relation to pregnancy and parturition is as old as the practice of obstetrics. Naturally, therefore, literature concerning this subject extends back to the ancients. Differences of opinion come to light most sharply for the first time in the attitude of Mauriceau and Madame Lachapelle. The former found that the labors of elderly primigravid women were longer and more severe than those of other primigravid women and that these patients more frequently suffered from eclampsia. He stated that the weight of the children was greater than normal and that the mortality rate among them was greater. Lachapelle on the contrary maintained an optimistic attitude and remarked that "no doubt one often observes a slow and painful labor in the older primigravidas, but is it not the same in all ages?" She ventured the opinion that the proportion will be about equal.

A similar division of opinion is somewhat apparent in the modern literature. To those interested in the subject we recommend the thesis of Lundh published in 1926 as an exhaustive, interesting, and instructive exposition. His material concerned 7,000 primiparas between the ages of 13 and 47 years. Briefly his conclusions indicated a history of delayed onset of menstruation among elderly primiparas; an increase in the incidence of toxemia; the highest incidence of premature labor among the younger group; an optimum for the duration of labor around the twenty-second year of life with a gradual increase after the age of 25 years, coinciding with an increased inefficiency of the uterus and rigidity of the soft parts, and with an increase in the incidence of operative delivery and damage to soft tissue. In the older group of parturients he found a prolongation of the third stage of labor with an increase of necessary intervention at that time. He reported no change in the weight, bodily length, or circumference of the head of the infants and no change in the ratio of sex among them. There was an increase of the number of twin pregnancies. He noted a considerable increase of infant morbidity and mortality rates.

A few articles have appeared in the past ten years on this subject but the latest discussion before this society was by Quigley in 1930. The matter attracted our attention several months ago when a primigravid woman 45 years of age passed through a pregnancy and parturition with the facility of a woman of 25 years, giving evidence perhaps that her physiologic age was more to be considered than her calendar age.

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A uniform definition for the elderly primigravid woman does not seem to exist. Definitions are based on the actual age of the patient and vary from those more than 30 years of age to those more than 35 years of age and in one instance to those more than 38 years of age. Accordingly, we selected data on three groups of primigravid patients from the records of the Mayo Clinic for comparative study: 250 who were 35 years of age or older, 516 aged 30 through 34 years and 792 who were less than 30 years of age. Those data that seemed pertinent and which offer bases for comparison are enumerated and discussed herein. A number of patients came to us for emergency care having had prenatal care elsewhere or none at all. In some cases attempts had been made to deliver the infant before the mother was admitted to our service, but except for an occasional comment these patients are not specially designated in the paper. As might be expected in any group of 1,558 gravid women numerous medical and surgical complications occurred, many only once or twice, and there seems to be no reason to catalogue all of them in this paper.

Among the medical and surgical complications certain items evidence an expected trend. In the group more than 30 years of age significant disease of the thyroid was present eleven times. Ten patients were found to have adenomatous goiter and one had exophthalmic goiter. Three of these patients underwent operation during pregnancy. Of the 250 patients 35 years of age or older four had carcinoma. One patient had undergone radical mastectomy previous to an uneventful pregnancy and parturition. She died five years later as the result of an accident. One patient was found to have carcinoma of the breast when she was in the seventh month of gestation. Radical mastectomy was performed and the infant was later delivered by cesarean section. The patient died three years later of carcinoma. Another patient underwent operation for adenocarcinoma of the rectum early in pregnancy and subsequently the infant was delivered by cesarean section. In one patient carcinoma in situ of the uterine cervix was discovered at the time of the postpartum examination and was treated by total abdominal hysterectomy.

The older women more often entered on pregnancy with an elevation of blood pressure than the younger women. At less than 30 years of age preexisting hypertension was found in only 1 per cent of patients; from 30 through 34 years of age it was found in 3.9 per cent, while after the age of 35 years 11.6 per cent of women were found to have an increase of blood pressure either before pregnancy occurred or very early in pregnancy. Thus, as would be expected, the vascular system becomes more vulnerable with age. Many women who have hypertension pass through pregnancy without incident if renal function remains normal but if toxemia becomes superimposed on a pre-existing hypertension a serious situation exists.

The incidence of toxemia of pregnancy increased with age. Those patients less than 30 years of age experienced it in 10.7 per cent of cases; from 30 through 34 years of age toxemia was a complication in 13.7 per cent, while of those 35 years of age or older 18.4 per cent suffered from toxemia. These patients having toxemia include all those in whom pre-eclampsia in its various degrees of severity developed. Two patients who had eclampsia, both in the two older groups, were admitted for emergency treatment. Our over-all incidence of toxemia is approximately 6 per cent but in this sample of 792 women less than 30 years of age from three separate years for comparison the incidence of toxemia was 10.7 per cent.

The behavior of the uterus and cervix during labor revealed some differences. Among those patients experiencing vaginal delivery were a number who were considered to have uterine inertia, either primary or secondary,

on whom Dührssen's incisions were performed or in whom it became necessary to complete the last 2 or 3 cm. of dilatation manually. Thus in those 792 patients less than 30 years of age uterine inertia was diagnosed 14 times, Dührssen's incisions were made in 3 cases and the dilatation of the cervix was completed manually in 2 cases, making a total of 19 cases (2.4 per cent) in which the behavior of the uterus and cervix constituted a complication of labor. Among the 516 patients from 30 through 34 years of age, uterine inertia occurred fifteen times, Dührssen's incisions were performed in six cases and manual completion of cervical dilatation was performed in three cases, a total of twenty-four cases (4.6 per cent). When the patient was 35 years of age or older, uterine inertia was considered present in six of 250 patients, Dührssen's incisions were made in four and in six manual completion of cervical dilatation was performed, a total of sixteen (6.4 per cent). These numbers are small but they indicate a trend.

One may also consider the efficiency of the uterus as reflected by two other conditions. Errors of rotation of the occiput were more frequently encountered among older than among younger women. Among the 792 less than 30 years of age 33 errors (4.2 per cent) of anterior rotation that necessitated correction were present, from 30 through 34 years of age this occurred in 10.4 per cent and it occurred in 27 (10.8 per cent) of those patients 35 years of age or older. These errors or failures of normal rotation were corrected by various means. The factor of inefficient expulsive effort with perhaps the additional one of resistant soft parts is further reflected by the increase of necessary intervention at a higher plane in the pelvis among women in the older age group. Thus, in the group of 792 women less than 30 years of age, a midforceps operation was performed in 10 cases (1.3 per cent); in the 516 women from 30 through 34 years of age, 38 (7.4 per cent) required this procedure, and when the patient was 35 years of age or older, 30 of 250 (12.0 per cent) underwent the midforceps operation.

Induction of labor by castor oil and Pitocin, rupture of the membranes, or insertion of a hydrostatic bag occurred more frequently among the older age group than among those who were younger. At ages less than 30 years induction of labor was performed in 34 (4.3 per cent) of 792 patients; from 30 through 34 years of age among 516 patients, 56 (10.8 per cent) underwent induction of labor and in those patients 35 years or older 33 (13.2 per cent) had labor induced. These inductions were performed most frequently in the presence of toxemia of pregnancy.

The spread of occurrence of premature separation of the normally implanted placenta and placenta previa did not seem significant among these patients. In our experience at the clinic placenta previa has occurred in primigravidas in 19 per cent and in multiparas in 81 per cent of all cases of placenta previa, so that the number of women among these groups who had placenta previa was too small to bear analysis. The incidence of manual removal of the placenta, postpartum hemorrhage, and postpartum insertion of an intrauterine pack was actually less in the older than in the younger women but the totals are too small to merit comparison.

Premature rupture of the membranes occurred in 53 (21.2 per cent) of the 250 women 35 years of age or older compared to a general average of 12 per cent in the younger groups. Contracted pelvis was found in 41 (16.4 per cent) of 250 women 35 years of age or older and in 56 (10.8 per cent) of the 516 women aged 30 through 34 years. This difference is probably not significant.

As would be expected, the incidence and significance of myomas of the uterus increased with age. Among the 792 women less than 30 years of age myomas were noted only 15 times (1.9 per cent) but in 3 of these patients

myomectomy was performed during pregnancy. In only 1 patient in this group did the presence of myomas enter into the indications for cesarean section. In the remaining 12 of these 15 patients the myomas had no significant effect on pregnancy or parturition.

Among the 516 women 30 through 34 years of age, 39 (7.5 per cent) were found to have demonstrable myomas in the uterus. Twenty-one of these 39 patients did not experience any complications of pregnancy, parturition, or puerperium that could be attributed to the myomas. The remaining 18 of the 39 experienced some complication such as myomectomy, postpartum hemorrhage, adherent placenta, or degeneration of the myomas, or underwent cesarean section.

When the patients were 35 years of age or older, 42 (16.8 per cent) of these 250 women gave evidence of significant myomas in the uterus. In 30 of these patients no serious complication could be attributed to the myomas. In 12 patients, however, various complicating factors arose such as were mentioned previously and in 2 patients cesarean hysterectomy was performed.

Table I reveals the methods of delivery among the three groups of patients. It is to be remembered that these patients cover a period from 1924 through 1945 and therefore represent a period of considerable change in obstetric practice. For example, the high forceps operation has ceased to be used but in earlier days it was occasionally the only alternative in certain cases. We have always restricted the indications for podalic version and extraction, as is evident. Breech extraction was performed in about the same percentage in each group, indicating that, unless definite cephalopelvic disproportion exists, infants can be born by breech in primigravid women in all age groups.

TABLE I. NUMBER OF DELIVERIES AMONG PRIMIGRAVID WOMEN BY METHOD OF DELIVERY

| METHOD OF DELIVERY | AGE OF WOMEN, YEARS | | | | | |
|---|---|---|---|---|---|---|
| | LESS THAN 30 | | 30 THROUGH 34 | | 35 OR OLDER | |
| | NUMBER | PER CENT | NUMBER | PER CENT | NUMBER | PER CENT |
| Spontaneous | 423 | 53.5 | 210 | 40.6 | 78 | 31.2 |
| Low or outlet forceps | 303 | 38.2 | 209 | 40.5 | 91 | 36.4 |
| Midforceps | 10 | 1.3 | 38 | 7.4 | 30 | 12.0 |
| High forceps | 0 | | 2 | 0.4 | 1 | 0.4 |
| Version and extraction | 0 | | 4 | 0.8 | 2 | 0.8 |
| Breech extraction | 32 | 4.0 | 34 | 6.6 | 13 | 5.2 |
| Cesarean section | 23 | 2.9 | 16 | 3.1 | 32 | 12.8 |
| Craniotomy | 1 | 0.1 | 3 | 0.6 | 3 | 1.2 |
| Total | 792 | 100.0 | 516 | 100.0 | 250 | 100.0 |

Cesarean section deserves further comment. We have always tried to individualize all treatment in obstetrics and have applied this principle to the use of the cesarean operation as well. The incidence of the operation among those women less than 30 years of age is 2.9 per cent; it increases to 3.1 per cent when the patient is from 30 through 34 years of age and rises sharply to 12.8 per cent among the patients 35 years of age or older. Our over-all incidence of cesarean section since 1934 is 3.5 per cent. It will be noted that the number of indications per operation also increases with age and that the type of indication changes (Table II). It is our policy to employ a test of labor when the character of the pelvic contraction is suitable for this procedure and this was carried out in six of the patients 35 years of age or older, five resulting in cesarean section and one in delivery through the vagina. Nine of the sixteen cesarean sections performed in the group from

30 through 34 years of age were preceded by a test of labor. Among women 35 years of age or older and more frequently when more than 40 years of age, the factors of number of years of marriage, lessened remaining years for reproduction, associated disease of the uterus, such as myomas, complicating vascular disease with or without toxemia, and coexisting or previous carcinoma will weight one's judgment and emphasize the factor of evidence of cephalopelvic disproportion as an indication for cesarean section.

TABLE II. INDICATIONS FOR CESAREAN SECTION IN PRIMIGRAVID WOMEN ACCORDING TO AGE

| INDICATIONS | AGE OF WOMEN, YEARS | | |
|---|---|---|---|
| | LESS THAN 30 (792 WOMEN) | 30 THROUGH 34 (516 WOMEN) | 35 OR OLDER (250 WOMEN) |
| Cephalopelvic disproportion | 13 | 7 | 15 |
| Breech presentation | 3 | 0 | 4 |
| Placenta previa | 0 | 1 | 3 |
| Myomas | 1 | 6 | 11 |
| Malposition | 1 | 5 | 1 |
| Toxemia | 4 | 0 | 4 |
| Vaginal atresia | 0 | 0 | 1 |
| Ovarian cyst | 1 | 0 | 1 |
| Diabetes | 1 | 3 | 0 |
| Brain tumor | 1 | 0 | 0 |
| Cesarean hysterectomy | 0 | 0 | 3 |
| Heart disease | 0 | 2 | 0 |
| Previous infertility | 1 | 0 | 1 |
| Radical resection of breast for carcinoma | 0 | 0 | 1 |
| Adenocarcinoma, rectum | 0 | 0 | 1 |
| Total | 26 | 24 | 46 |
| Operations | 23 (2.9 per cent) | 16 (3.1 per cent) | 32 (12.8 per cent) |

Naturally, the number of patients having significant myomas increases with age, as mentioned previously, and, though myomas were not usually the sole reason for section unless they produced obstruction to the birth canal, they were often an added reason for the operation. Cesarean hysterectomy was performed twice because of myomas and once because of a couvelaire uterus associated with hemorrhage into the broad ligament.

Toxemia alone, except in an occasional instance of fulminating toxemia that does not respond to treatment, particularly when the cervix is not ripe, is rarely considered an indication for section at the clinic. This condition became the indication or one of the indications in 8 of the total of 71 cesarean operations in all three groups.

The remainder of the indications need no comment. It is to be noted that in the older age groups multiple indications were frequently present. The only maternal death in all groups was that of a primigravida aged 43 years on whom a classic cesarean section was performed in 1933 for central placenta previa and who died on the third postoperative day, the diagnosis being peritonitis and paralytic ileus. No necropsy was obtained.

Six reports concerning elderly primigravidas which appeared between 1931 and 1944 were taken at random. The fetal mortality rate averaged 6.1 per cent. The incidence of cesarean section averaged about 14 per cent, though this average perhaps is not truly representative, for there was great variation of the incidence. The maternal mortality rates after cesarean section likewise differed greatly. The six reports listed no deaths in one group of 31 patients[2] who underwent cesarean section, no deaths in 35 patients,[8]

three deaths in thirteen cases,[9] two deaths in eleven cases,[1] three deaths in 56 cases,[3] and five deaths in 111 cases.[4] This represents thirteen (5.1 per cent) deaths in 257 elderly primigravidas who underwent delivery by cesarean section, a figure higher than we had anticipated. The cases reported in these six groups of patients total 1,780. Cesarean section was performed in 257 cases, an incidence of 14 per cent. It must be remembered, however, that these reports concern long periods and many of these cesarean sections no doubt were performed before modern techniques and safeguards were available.

Our own instance of death after cesarean section occurred under these circumstances. If we consider all patients 30 years of age or older, this one death gives us an operative mortality rate of 2 per cent; if only those 35 years of age or older are included (this patient was 43 years of age), the mortality rate is 3.1 per cent. We have performed more than 400 consecutive cesarean sections since 1934 without a death. Certainly chemotherapy, antibiotics, the blood bank, low cervical and extraperitoneal cesarean section have contributed to this record.

One of the most significant items in this study concerns the fetal mortality rate. The figures shown in Table III are uncorrected. It is obvious that, if the intrauterine deaths alone were excluded, an appreciable alteration would be made. The fetal mortality rate was more than three times as great among infants born to mothers 35 years of age or older compared to those born to mothers less than 30 years of age. This increase seems to correlate with the increase in cases of toxemia and to relate also to the incidence of prematurity but in many instances the cause could not be accurately determined, particularly in premature macerated fetuses. Table III also reveals that the number of infants weighing less than 2,500 Gm. at birth increases very appreciably among the older group of patients. The 31 cases (12.4 per cent) in which the mother was 35 years of age or older are influenced by the increased incidence of induction of labor mentioned previously and by the intrauterine death of premature infants.

TABLE III. MORTALITY RATE OF INFANTS BORNE BY PRIMIGRAVID WOMEN ACCORDING TO AGE OF MOTHER, AND NUMBER OF INFANTS WEIGHING LESS THAN 2,500 GM. AT BIRTH

| | AGE OF MOTHER, YEARS | | | | | |
|---|---|---|---|---|---|---|
| | LESS THAN 30 (792 WOMEN) | | 30 THROUGH 34 (516 WOMEN) | | 35 OR OLDER (250 WOMEN*) | |
| DEATH OF INFANT | INFANTS | PER CENT | INFANTS | PER CENT | INFANTS | PER CENT |
| Before onset of labor | 8 | 1.0 | 16 | 3.1 | 14 | 5.6 |
| During labor | 8 | 1.0 | 5 | 1.0 | 4 | 1.6 |
| Neonatal | 6 | 0.8 | 5 | 1.0 | 5 | 2.0 |
| Total | 22 | 2.8 | 26 | 5.1 | 23 | 9.2 |
| Infants less than 2,500 Gm. at birth | 46 | 5.9 | 34 | 6.6 | 31 | 12.4 |

*One pair of twins, making 251 infants.

Analysis of the infant mortality rate in the two groups of older women reveals that, of the 516 children born to mothers aged from 30 through 34 years, 26 did not survive (Table III). None of these may be charged to the delivery. Three infants suffered from hydrocephalus and three from anencephalus. Twelve infants were macerated when stillborn but did not reveal gross defects. Two infants died before the onset of the second stage of labor, one in association with severe toxemia in the mother and in one case delivery had been attempted elsewhere and the infant was dead on admission to the hospital. One infant was stillborn at the time of cesarean section. Five infants died during the neonatal period, all weighing well under 2,500 Gm.

Twenty-three of 251 infants born to the 250 women 35 years of age or older did not survive. Four of these deaths may be charged to operative vaginal delivery. In one instance forceps delivery failed in a case of cephalopelvic disproportion, the infant died in the second stage of labor and craniotomy was performed. A difficult midforceps operation resulted in a stillborn infant in one case. One infant died in the neonatal period after a low forceps delivery but postmortem examination was not permitted. The last of these four infants died during a version and extraction. In four infants hydrocephalus was present and in one anencephalus was found. Seven infants were macerated when born. Twins, weighing 1,000 Gm. each at birth, died during the neonatal period. One infant succumbed to erythroblastosis. Three infants died in the uterus but were born before maceration occurred and one infant died as a result of prolapse of the umbilical cord.

The expected date of confinement is not calculated without error. The obstetrician uses other criteria to estimate the ripeness of a pregnancy but to the patient the calculated date assumes much importance. We have checked this date against the fetal mortality rate. The results indicate that postmaturity calculated on this basis assumed no importance in the fetal mortality rate but that prematurity greatly influenced fetal salvage.

As has been indicated previously, those who have written concerning the elderly primigravid woman have approached the subject from variable points of view. This variation probably stems from the occurrence that motivated the construction of a paper on the subject. One develops a plan or philosophy of the practice of medicine generally and obstetrics in particular, partly from the experience of others but largely from the happenings in one's own experience. Whatever discussion we may state is so predicated. Perhaps impressions would be a better term and others may construe it variously.

Certain conditions may be expected to occur in any group of older women. Accordingly, adenomas of the thyroid, pre-existing hypertension, myomas of the uterus, and carcinomas were more evident among them than in a comparable younger group of obstetric patients.

We encountered more toxemias of the latter months of pregnancy among older primigravid women than among younger women and more frequently were forced to induce labor prematurely because of this condition. One of the components of these toxemias is arteriolar spasm, which must be more poorly borne by a patient who suffers from pre-existing hypertension. Needless to say, meticulous prenatal care and early recognition of, and adequate treatment for, these toxemias are of great importance.

The efficiency of behavior of the genital tract during parturition seems to us to decline with advancing years. Replacement of the musculature of the uterus by myomatous tissue probably plays a part as well as a diminution of the elasticity of the soft tissues of the pelvis. The increase of dysfunction of the uterus and cervix, the increase of failures of rotation of the occiput and the larger number of operative procedures at a higher level in the birth canal bespeak this lack of efficiency. Perhaps the larger percentage of patients experiencing premature rupture of the membranes belongs in this same category. There was an increase of the number of patients whose pelvic diameters were smaller than normal, as has been noted by others. This increase, though small, assumes added significance when related to the factors mentioned previously. All of these involve an increased risk to the mother. In competent hands this should be minimal but we know that maternal morbidity and mortality rates tend to increase as the incidence of operative delivery mounts.

Various reasons are given for the increased performance of cesarean section among these older women. One reason relates to the value of the infant

under circumstances of a lessened remaining period of reproduction and associated disease or lessened functional capacity of the pelvic viscera. These conditions naturally are found with increasing frequency as aging occurs and, when associated with other factors such as toxemia or contraction of the pelvis even though these may not be severe, lead one to consider cesarean section. In our experience, in nearly 90 per cent of women 35 years of age or older the infant was delivered through the vagina; but four deaths among the 23 infants who died must be charged to operative delivery and the infants might have survived had cesarean section been performed. Perhaps minor degrees of bony pelvic contraction have been overemphasized and the unelastic soft tissues equally at fault have not been considered in selecting the method of delivery. If uterine behavior, errors of rotation, and the necessity of intervention higher in the birth canal are increased accompaniments of vaginal delivery, then one again must carefully weigh the decision as to method of delivery. We believe that an incidence of cesarean section of 12.8 per cent in the group 35 years of age or older is justified. We also believe that each case should be given comprehensive individual consideration and that age alone is not the sole criterion.

Our experience would indicate that, unless some complication necessitates the induction of labor, the pregnancy should not be disturbed until the spontaneous onset of labor. Assuming that the possibility of cephalopelvic disproportion is carefully considered, it would seem that the best interests of mother and infant are served if labor occurs when the cervix is ripe and the uterus is ready to function. Accidents and complications related to the placenta occurred no more frequently among the older women than when the patient was young. If one applies in full the advantages of modern prenatal care and scrutinizes the elderly primigravid woman carefully and further applies appropriate care at the time of delivery with all of our present-day protections, it would seem that these patients may undertake pregnancy and parturition with minimal risk.

We may not be satisfied with our fetal salvage. The frequent necessity of inducing labor with the resultant prematurity of the infant, the number of infants born weighing less than 2,500 Gm., and the associated toxemia in the mother, together with exposure to major obstetric operative procedures through the vagina, serve to increase the hazard to the infants born to elderly primigravid women. In our experience postmaturity or the oversized infant did not contribute significantly to infant deaths. An uncorrected fetal mortality rate of 9.2 per cent of children born to mothers aged 35 years or older must be compared to an uncorrected fetal mortality rate of 2.8 per cent when the mother is less than 30 years of age. On occasion these factors will lead to the performance of cesarean section in the interest of the infant. Age of the mother alone seems rarely a sufficient reason for cesarean section but should be one of the factors to be considered.

## Conclusions

General bodily conditions related to aging will appear more frequently in elderly primigravidas. Reduced efficiency of the genital tract becomes apparent from the increased number of patients who have myomas of the uterus. More frequently one encounters the combination of uterine inertia and delay in dilatation of the cervix in these patients.

Because of these factors and an increase of frequency of contraction of the bony pelvis and resistance of the soft tissues in the pelvis, operative

intervention at a higher level in the pelvis was more often necessary among older patients.

Cesarean section has an increased place in the delivery of infants among elderly primigravidas but the indications should be carefully considered and individualized. An incidence of 12.8 per cent for the performance of cesarean section seemed justified in this group of patients.

Prenatal care is now well standardized among well-trained obstetricians but these principles must be applied with increased care to elderly primigravidas, for they experience an increased incidence of toxemia.

In our experience the infant bears the major risk when pregnancy occurs in elderly primigravid women.

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## Discussion

DR. JOHN H. MOORE, Grand Forks, North Dakota.—Dr. Randall's study of a group of obstetric patients, whom he designated as elderly primigravid women, has resulted in some interesting conclusions. My attitude is that of Madame La Chapelle, rather than that of Mauriceau. I am completely in accord with the statement of the essayist that "physiologic age was more to be considered than calendar age."

I was surprised to find Dr. Randall classifying 516 patients in his thirty to thirty-four years age group as "elderly primigravid women." The Twentieth Century Dictionary defines "elderly" as, "Somewhat old; advanced beyond middle age; bordering on old age." If I were an obstetric patient, even in the thirty-five to forty-plus age group, I think I would resent the adjective "elderly." If the term persists, we may find ourselves speaking of such an inconsistency as geriatric obstetrics!

A review of 1,624 consecutive obstetric patients, delivered in the Grand Forks Clinic between Jan. 1, 1940, and Dec. 31, 1947, showed 544 who were primigravid. In Dr. Randall's series of 1,558 primigravid women, there were 250 who were 35 years of age or older to our 23; he had 516, aged 30 to 34 years as compared with our 63; and 792 of his patients were under the age of thirty in contrast to our 458. We had no malignancies in our series.

Taking the length of the first stage of labor as a guide, I was unable to differentiate between the behavior of the uterus and cervix in any of our three groups. From the youngest to the oldest of the three groups this averaged 12 hours, 11 hours, and 12 hours and 21 minutes.

Dührssen's incisions and manual dilatation of the cervix which, in our hands, I would be forced to call manual laceration of the cervix, were not employed.

Cesarean section is important in this study. In the twenty-year period, covered by Dr. Randall's report, the incidence of cesarean section was 2.9 per cent in the women

under 30; 4.26 per cent in the patients between 30 and 34 and 12.8 per cent among the patients over 35 years of age. In our eight-year report I found 3.9 per cent; 9.5 per cent and 13 per cent, respectively. His over-all incidence of cesarean section since 1934 was 3.5 per cent; ours, during the past eight years was 4.9 per cent.

We had an uncorrected fetal mortality of 1.5 per cent in our 458 patients under the age of 30; 3.5 per cent in the 63 patients between 30 and 34, and none in the 23 patients over the age of 35 years.

Pre-existing hypertension became clinically important in two of our twenty-three patients over the age of 35 years; and two other patients in this group had uterine myoma and/or adenomyosis which required surgical section. The myoma developed acute red degeneration for which a myomectomy was done late in the eighth month of pregnancy, with subsequent delivery per vaginam at term. No myomas of clinical significance were found in any of our patients in the 30 to 34 age group or in those under thirty.

In the 544 primiparous patients in our series, the incidence of late toxemias of pregnancy was 2.6 per cent and in the 1,624 patients, covered by the same eight-year period, the incidence was 5 per cent. There were no maternal deaths in the primigravid group and one among the 1,624 patients.

Dr. Randall has indicated that cesarean section has an increased importance in the delivery of primigravid patients 35 years of age or older and has suggested factors, other than bony pelvis contraction, which may make cesarean section more desirable in this group. Our statistics in percentage are almost identical for cesarean section in this group. Contraction of the bony pelvis, however, accounted for all of our cesarean sections in the 30 to 34 age group and in all but two in the group under 30 years.

In conclusion, may I suggest that we substitute the adjective, "discriminating" for "elderly" in describing that fine group of patients who, having reached the age of discretion, which Dr. Randall places at thirty years or over, decide to have their first babies.

DR. BUFORD G. HAMILTON, Richmond, Mo.—I have selected 706 cases for discussion, cared for personally through the years. Like Dr. Randall, I have divided these cases into three groups for study. Two hundred forty-eight were 30 to 35 years of age, 108 were 35 to 44 inclusively, and 350 were under the age of 30.

EVENTS IN THE LABOR OF PRIMIGRAVID WOMEN AS TO AGE

| | 350 WOMEN UNDER 30 YEARS OF AGE | 248 WOMEN FROM 30 TO 34 YEARS OF AGE | 108 WOMEN OVER 35 YEARS OF AGE |
|---|---|---|---|
| Pulse (befrore and after labor) | 82.27-89.82 | 83.35-90.27 | 84-97 |
| Duration of labor | 16.02 hours | 14.36 hours | 15.34 hours |
| Blood loss | 162.2 c.c. | 163.59 c.c. | 201.3 c.c. |
| Dilatation completed | 6 | 8 | 3 |
| Induction | 3 | 3 | 4 |
| Third degree tear | 1 | 1 | 1 |
| Weight of baby | 7.37 pounds | 7.42 pounds | 7.5 pounds |
| Deaths of mothers | 1 (anesthetic) | 1 (toxemia) | 0 |
| Toxemias | 18 (5.14%) | 24 (9.7%) | 10 (9.3%) |

MORTALITY OF BABIES

| | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT |
|---|---|---|---|---|---|---|
| Before labor | 7 | 2.0 | 9 | 3.63 | 2 | 1.6 |
| During labor | 8 | 2.3 | 3 | 1.2 | 1 | 0.9 |
| After labor | 5 | 1.43 | 4 | 1.61 | 2 | 1.6 |
| Premature | 7 | 2.0 | 4 | 1.61 | 4 | 3.7 |

METHOD OF DELIVERY AMONG PRIMIGRAVID WOMEN

| | 350 WOMEN UNDER 30 YEARS OF AGE | | 248 WOMEN FROM 30 TO 34 YEARS OF AGE | | 108 WOMEN OVER 35 YEARS OF AGE | |
|---|---|---|---|---|---|---|
| | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT |
| Spontaneous | 165 | 47.0 | 103 | 41.5 | 42 | 38.89 |
| Low forceps | 121 | 34.6 | 116 | 46.77 | 45 | 41.6 |
| Midforceps | 26 | 7.42 | 5 | 2.01 | 3 | 2.77 |
| High forceps | 1 | 0.28 | 1 | 0.4 | 0 | 0 |
| Manual rotation | 20 | 5.7 | 10 | 4.03 | 2 | 1.8 |
| Version | 6 | 1.7 | 5 | 2.0 | 4 | 3.73 |
| Breech extraction | 28 | 8.0 | 15 | 6.0 | 9 | 8.25 |
| Cesarean section | 3 | 0.85 | 3 | 1.2 | 5 | 4.6 |
| | 350 | | 248 | | 108 | |
| (Twins | 3 | 0.85%) | 3 | 1.2%) | 1 | 0.92%) |

INDICATIONS FOR CESAREAN SECTION IN PRIMIGRAVID WOMEN ACCORDING TO AGE

| | 350 WOMEN UNDER 30 YEARS OF AGE | 248 WOMEN FROM 30 TO 34 YEARS OF AGE | 108 WOMEN OVER 35 YEARS OF AGE |
|---|---|---|---|
| Cephalopelvic disproportion | 1 | 0 | 0 |
| Breech | 0 | 1 | 1 |
| Placenta previa | 1 | 1 | 1 |
| Myomas | 1 | 0 | 1 |
| Toxemias | 0 | 1 | 1 |
| Abruptio placentae | 0 | 0 | 1 |
| | 3 (0.85%) | 3 (1.2%) | 5 (4.6%) |

Efficient prenatal care should develop an appreciation of the physiological, the anatomical and the psychological responses of each patient. The evolution in training should so develop one's conception of the merit of procedure that the age factor would be eliminated.

DR. L. A. CALKINS, Kansas City, Kan.—I can agree heartily with all that Dr. Randall has said, but I should like to say it in a different way. The woman who is young enough to become pregnant is young enough to go through the complete physiology of having her baby. The older women are old enough to have developed complications in other parts of the body just as Dr. Randall has stated; heart disease, myoma, carcinoma; etc. I would like to disagree with Dr. Randall in his selection of primigravid women, as I believe that the multigravid woman has the same increased risks as the primigravid woman.

DR. J. BAY JACOBS, Washington, D. C.—Dr. Quigley stressed the fact that most obstetricians and patients, and of course the families, were greatly concerned because of the age of the patient and attendant disagreeable factors that perhaps have been exaggerated, especially in the opinion of the patient.

Davis recently published an article entitled, "Childbearing in the Twilight of the Reproductive Period," in which he included primiparas as well as multiparas, and found that pregnancy complications for both mother and baby were increased in these women. We can compare his figures very effectively with those of Dr. Randall's group. Even in multiparas, the complications increased somewhat in the older age groups.

There are some factors that we must be aware of. The elderly primipara presents a mental attitude different from that of the young woman and I personally feel that that may affect the character of her labor and, of course, Dr. Randall had referred to this factor as some of the previous speakers had. We also are concerned with the type of labor the elderly primipara has. Personally, I do not feel that the uterus would contract so effectively in an old primipara as in a young one. Certainly in most cases it does not, and

I think the incidence of contracted pelvis is probably a little greater in elderly primiparas than in the young ones. Perhaps this, along with the absence of other typically feminine characteristics, is the reason why the woman is an elderly primipara rather than a young one. In other words, she may lack the necessary factors that tend to encourage early marriage.

In handling these cases, in spite of the good reports that have been shown, the morbidity and mortality rate for the mother, as well as for the fetus, is the thing that causes the most concern to the patient and her family. Her mental attitude naturally will be affected by the outcome. Even though these women are initially physiologically elderly, after the baby is born their mental and physical attitude is changed entirely, they appear and react as younger women do, and are anxious to have more babies, if the outcome is good. On the other hand, we must remember that if the outcome is not so good the mental attitude will become worse and quite serious for the patient.

I want to stress one thing in dealing with elderly primiparas. I do not hesitate to say that I am concerned. When confronted with an elderly primipara, I feel almost as I would if a young primipara of 200 or 220 pounds, with the disagreeable factors that generally attend such cases, walked into my office for the first time. In other words, I have particular concern for the elderly primipara regardless of the fact that such excellent results are reported. The thing that we are confronted with is primarily the mental attitude of the individual, and the responsibility involved because of the effect of that mental attitude upon the processes of pregnancy and labor, along with possibly some pelvic contraction, or other disagreeable factors.

The question is, how will labor progress in these individuals? I feel these women are entitled to a test of labor, but not the prolonged test that you would allow the young women to have. In the absence of serious complications, I would determine just how the uterus behaves during labor. If the contractions were effective and regular and there was no tendency to develop inertia, I would allow an effective test of labor; if there were any question, would do an elective cesarean section.

DR. JAMES K. QUIGLEY, Rochester, N. Y.—I have been inclined to advance the age limit from 30 to 35 as to what constitutes the elderly primipara. I would be interested to know whether Dr. Randall's cases carried with them an added risk to the mother and her baby. I believe Dr. Calkins has pointed out that the elderly multipara often has the same risk as the primipara.

DR. RANDALL (Closing).—The comment made by Dr. Calkins is pertinent but we did not cover that aspect of it in the paper. We have always used a trial of labor in selected cases and that was done in women in this group.

*(The papers of Dr. Schmitz, Dr. Schwarz, and Dr. Quigley, presented at this meeting, will be included in the next issue of the* JOURNAL.*)*

# Item

## Fellowships for Cytological Diagnosis Course

The American Cancer Society is offering two fellowships for a four-month course in the study of exfoliative cytology at the laboratories under the supervision of Dr. Herbert F. Traut, Dr. James F. Rinehart, and Dr. Seymour M. Farber, in the University of California Medical School. Half the time is to be spent at the laboratory in the University of California Hospital and the other half at the San Francisco County Hospital cytology laboratory.

The fellowships include a payment of tuition fee and overhead to the University, and the trainee will receive $140.00 per month to partially cover his living expenses for the period.

The requirements for the fellowships are that the applicants:

1. Be graduates of Class A Medical Schools of the United States, its territories, or of Canada.
2. Be citizens of the United States.
3. Be not over fifty years of age.
4. Have completed two years of postgraduate training in pathology.

The instruction will be given by three physicians who are experienced in the method and are spending full time in the work, and by six experienced technicians. There will be intermittent periods of personal instruction but no classes. The rest of the time will be spent in the study of the available classified material and the current specimens.

Please address inquiries to:

Milton Rosenthal, M.D.,
Office of Medical Extension,
University of California Medical Center,
San Francisco 22, Calif.

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**Mull-Soy is a liquid hypoallergenic food prepared from water, soy flour, soy oil, dextrose, sucrose, calcium phosphate, calcium carbonate, salt, and soy lecithin; homogenized and sterilized. Available in 15½ fl. oz. cans at all drugstores.**


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# Mull-soy

When Milk becomes "Forbidden Food"